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JOURNAL OF GENERAL CHEMISTRY OF THE USSR

Volume 28, Number 4 April 1958

CONTENTS

	PAGE	RUSS. PAGE
Basic and Acidic Oxides of Metals of the Large Periods of the Periodic System. S. A. Shchukarev	819	845
The Dissociation Constants of Trihydroxyglutaric Acid. N. K. Davidenko	832	859
Physicochemical Investigation of the Interaction of Acetone with Acetic Acid and Its Derivatives. I. M. Bokhovkin	835	862
Investigation of the Interaction of Diphenylamine with Organic Acids by the Methods of Physicochemical Analysis. N. K. Tsvetkova and D. E. Dionis'ev	840	868
Physicochemical Analysis of the System Ethylenediamine–Allyl Mustard Oil. M. P. Dianov and N. A. Trifonov	845	872
Ethylene Sulfide in the Synthesis of Heterocyclic Compounds with Two Hetero-Atoms. VII. 3-Arylthiazolidine-2-carboxylic Acids and Their Derivatives. Iu. K. Iur'ev and S. V. Diatlovitskaia	848	875
Reaction of 1,3-Dichlorobutene-2 with Isoprene and Divinyl Under the Influence of $FeCl_3$. III. A. L. Klebanskii, A. G. Saiadian, and M. G. Barkhudarian	853	881
1,4-Hydroxyketones and 1,4-Diketones in the Catalytic Synthesis of Homologs of Δ^2-Pyrroline and Δ^2-Dihydrothiophene, and, Correspondingly, Homologs of Pyrrole and Thiophene. Iu. K. Iur'ev and N. V. Makarov	857	885
Heterocyclic Derivatives of Methyl Ketones. F. N. Stepanov and S. L. Davydova	864	891
Synthesis and Reactions of Some Thiazolidine Derivatives. I. Preparation of Azorhodanines. A. P. Grishchuk and S. N. Baranov	869	896
Investigation of the Chemistry of Organic Oxides. XIV. Reaction of the α-Oxide of Isoprene with Ammonia and Amines. V. M. Al'bitskaia and A. A. Petrov	873	901
Investigation of Isomerization and Dimerization of Dimethylvinylcarbinol Relative to the pH of the Reagent. III. The Effect on Dimethylvinylcarbinol of Hydrochloric Acid, Saturated with Sodium and Magnesium Chlorides, and Hydrofluoric Acid. A. I. Lebedeva and L. F. Almashi	876	904
Investigation of Ethers with a Double Bond in the Allyl Position. III. Study of the Etherification of $\alpha,\alpha,\gamma,\gamma$-Tetraalkyl Substituted Allyl Alcohols. V. I. Pansevich-Kolíada and I. F. Osipenko	881	909
Investigation of Oxido Compounds. XI. Reaction of α-Oxides of Allyl Ethers of Phenol, p-Cresol and Guaiacol with Methyl Alcohol. V. I. Pansevich-Kolíada and Z. B. Idel'chik	887	914
The Abnormal Products of Vinyl-1-Cyclohexene-3 Ozonolysis. A. I. Iakubchik, A. I. Spasskova, and B. I. Tikhomirov	890	916

CONTENTS (continued)

	PAGE	RUSS. PAGE
Synthesis of Acetic Ester of Bis(Hydroxycyclohexyl)-1,3-butadiyne and Its Catalytic Hydrogenation. A. I. Nogaideli and G. M. Gonadze	895	921
Ethers of Glycols and Their Derivatives. XXXII. Synthesis of Monoethers of γ-Glycols and Their Alkoxymethyl Derivatives. Shamkhal Mamedov and A. F. Aliev	897	923
Diamines of Benzimidazole Series. I. Synthesis and Physicochemical Properties of Diamines. B. A. Porai-Koshits and Ch. Frankovskii	902	928
Diamines of Benzimidazole Series. II. Substantive Properties of the Azo Dyes Derived from the Diamines. B. A. Porai-Koshits and Ch. Frankovskii	908	934
Addition of Neutral Esters of Phosphorous and Phosphonous Acids to Conjugated Systems. IV. Addition of Esters of Phenylphosphonous Acid to α,β-Unsaturated Aldehydes and Acids. Gil'm Kamai and V. A. Kukhtin	913	939
Imidazole Derivatives. XX. Some Amino Derivatives of Benzimidazolone. L. S. Efros and A. V. El'tsov	916	941
Organomagnesium Synthesis and Properties of 1,1,1-Triphenylalkylmethanes, 1,5-Diphenyl-3-Benzylpentane, and 1-Phenyl-3-(2-Phenylethyl) Tridecane. II. M. A. Chel'tsova, A. D. Petrov, and Iu. P. Egorov	920	945
Reaction of Exchange of Hydroxyl Groups for Radicals of Organomagnesium Compounds. II. Reaction of Grignard Reagent with Symmetric Acetals. M. F. Shostakovskii and M. R. Kulibekov	926	951
Steric Hindrance in Organomagnesium Reactions. XVIII. Synthesis of Esters of α-(β-Alkoxy-1-naphthyl) Lactic Acids. I. I. Lapkin and V. Ia. Vlasova	930	955
Steric Hindrance in Organomagnesium Reactions. XIX. Synthesis of Esters of α-(4-Alkoxy-1-naphthyl) Lactic Acids. I. I. Lapkin and O. M. Lapkina	933	957
Heterocyclic Compounds. 61. Synthetic Analgesic Substances. XXV. Esters of 1,2,5-Trimethyl-4-phenyl (aryl)-4-piperidol. I. N. Nazarov, N. S. Prostakov, and N. N. Mikheeva	936	960
Synthesis of N-Methyl-3-carbomethoxy-4-hydroxypiperidines and a Study of Their Steric Structures. M. E. Maurit and N. A. Preobrazhenskii	943	968
Chemistry of Heterocycles. XXXII. Di- and Polyhalo Derivatives of 9-Phenylacridine with Positions of Halogen in Different Benzene Rings. M. E. Konshin and P. A. Petiunin	949	974
Study of the Stephen Reaction. M. M. Shemiakin, V. I. Maimind, B. V. Tokarev, and V. I. Karpov	952	978
The Polymeric Peroxide of Vinyl Chloride. G. A. Razuvaev and K. S. Minsker	957	983
Reaction of Aromatic Compounds with Alcohols in the Presence of Acid Catalysts. IV. Reaction of Benzene with Polyhydric Alcohols in the Presence of Acid Catalysts. I. P. Losev and O. V. Smirnova	965	991
Reaction of Aromatic Compounds with Alcohols in the Presence of Acid Catalysts. V. Reaction of Benzene with Polyvinyl Alcohol in the Presence of Acid Catalysts. I. P. Losev and O. V. Smirnova	968	994

CONTENTS (continued)

	PAGE	RUSS. PAGE
Internal Complex Salts of Azo Compounds. V. Coppering of o-Hydroxy-o'-alkoxyazo Compounds with Simultaneous Dealkylation. V. I. Mur	972	998
Dipolar Ions, Formed by the Elimination of a Proton from an NH Group. XII. Derivatives of 6-Quinolinesulfonic Acid. A. M. Simonov	976	1003
Condensation of 6-Quinolinealdehyde with Ketones and Esters. B. P. Lugovkin	980	1007
Reaction of Diazo Compounds with Sulfamic Acid and Its Derivatives. IX. Reasons for the Color of Diazonium Salts of Arylsulfamic Acids. D. Z. Zavel'skii and L. A. Lishnevskaia	983	1010
Reaction of Hydrazine with Nitro Compounds of the Anthraquinone Series. II. Synthesis of Vat Dyes – Derivatives of Pyrazoleanthronecarboxylic Acid. N. S. Dokunikhin and I. D. Pletneva	991	1019
Azo Derivatives of Cyanine Dyes. A. I. Kiprianov and I. P. Fedorova	994	1023
The Reaction of Hydrazine with Carbon Disulfide Experiments on the Synthesis of Diisothiocyanogen. A. Ia. Iakubovich and V. A. Ginsburg	1002	1031
A Method of Obtaining Fluorine Derivatives of Silicon, Tin, and Sulfur. A. A. Iakubovich, S. P. Makarov, and V. A. Ginsburg	1006	1036
The Tautomerism of 9-Aminoacridine. A. K. Sukhomlinov	1009	1038
The Synthesis of 5,6,7-Trimethylisoalloxazines. V. M. Berezovskii and E. P. Rodionova	1016	1046
Esters of Aminophenylsulfonamidophosphoric Acid. A. V. Kirsanov and N. G. Feshchenko	1020	1049
Triaryloxyphosphazosulfonalkyls and Aromatic Esters of Alkyl Sulfonamidophosphoric Acids. A. V. Kirsanov and N. L. Egorova	1023	1052
Substances with Complex Forming Ability. II. Trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic Acid and Trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic Acid. V. G. Iashunskii	1026	1056
Cyanoethylation of Aryl Sulfonamides. A. E. Kretov and N. P. Romazanovich	1029	1059
Synthesis of the Diethyleneimide of 4-Methyluracil 5-Methylene Phosphinic Acid. A. Ia. Berlin and M. N. Vasil'eva	1033	1063
Studies in the Field of Synthesis and Polycondensation of N-Alkyl Derivatives of Hexamethylenediamine. I. Synthesis of N,N'-Dialkyl Derivatives of Hexamethylenediamine. D. L. Klebanskii and M. S. Vilesova	1036	1066
Research in the Field of Synthesis and Polycondensation of N-Alkyl Derivatives of Hexamethylenediamine. II. The Synthesis of N-Monoalkyl Derivatives of Hexamethylenediamine. A. L. Klebanskii and M. S. Vilesova	1042	1073
Synthesis of Alkoxy-Substituted Ketones of the Isoquinoline Series. L. I. Linevich	1045	1076
The Action of Nitrous Acid on Cyclic Salts of Salicylic Acid. The Preparation of 5-Diazosalicylic Acid. A. A. Nemodruk	1051	1082
Dimethyl Arylsulfon-N-methylamidophosphates. V. I. Shevchenko and G. I. Derkach	1054	1085
Alkaloids of Peganum Harmala L. II. The Structure of Two New Alkaloids. N. I. Koretskaia and L. M. Utkin	1056	1087

CONTENTS (continued)

	PAGE	RUSS. PAGE
Investigation in the Field of Indole Derivatives. V. The Problem of the Mechanism of the Fischer Reaction. N. N. Suvorov, N. P. Sorokina, and Iu. N. Sheinker	1058	1090
The Synthesis of Tropane-3-α-ol, Tropine. G. I. Bazilevskaia, D. V. Gura, M. S. Bainova, K. M. Diumaev, I. K. Sarycheva, and N. A. Preobrazhenskii	1065	1097
Reactions of Magnesylamines. V. The Mechanism of the Reaction of Aryl Amidation of Aromatic Aldehydes by N,N-Bis-(Magnesium halide)-Aryl Amines. P. A. Petiunin and L. A. Tetiueva	1072	1105
The Occurrence of Equilibrium of Three Liquid Phases in Ternary Systems. I. L. Krupatkin	1075	1108
The Causes of the Transposition of Metals in the Electromotive Force Series in Fused Electrolytes. Iu. K. Delimarskii	1079	1112
In Memory of Andrei Ivanovich Lun'iak	1084	1118
Letter to the Editor. G. Chiurdoglu, Ch. Goldenberg, and J. Geeraerts	1086	1120

BASIC AND ACIDIC OXIDES OF METALS OF THE LARGE PERIODS OF THE PERIODIC SYSTEM*

S. A. Shchukarev

A useful approach to the problem of thermodynamic characterization of the basic and acidic functions of oxides is the comparison of the energy relations of pleiads of halides, especially chlorides, of a given element with the energetics of pleiads of the corresponding oxides. Such a comparison may provide data for an answer to the question: which oxides are bound to be basic (susceptible to neutralization by hydrochloric acid with formation of chlorides that are not hydrolyzable by water) and which, conversely, are not susceptible to neutralization, i. e., are acidic so that the chlorides are acid chlorides and easily hydrolyzed?

The energetic characterization is of course not the only useful approach, and an important light on the problem of basicity and acidity of oxides is thrown by the theory of transition from compounds with an ionic bond to compounds with a covalent bond; useful information is also provided by reactions of oxides with water. Nevertheless, thermodynamic relations can play a big part, if only because of the abundance of experimental data.

As a concrete example, we shall examine the behavior of vanadium, which gives, in the higher valence stages, V_2O_5, VF_5, VCl_4, VBr_3 and VI_2.

In Fig. 1 oxidation stages are plotted on the abscissas and the enthalpies of formation on the axis of the ordinates.

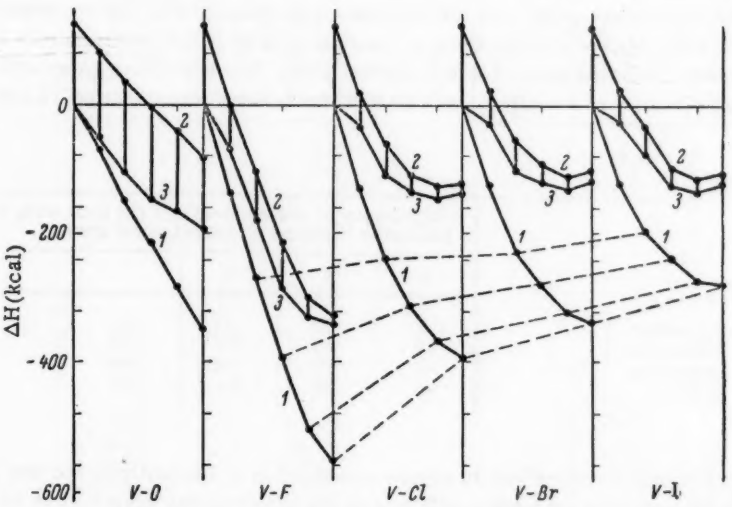


Fig. 1. Dependence of energy of formation of oxides, fluorides, chlorides, bromides and iodides of vanadium on the stages of oxidation (calculated per g-atom of metal). 1) Formation of gaseous compounds from free atoms; 2) formation of gaseous compounds from simple substances; 3) formation of solid compounds from elements. The differences between the ordinates of points of lines 2 and 3 are equal to the enthalpies of condensation.

* Preceding communication, see [1].

We see from Fig. 1 that the energy of condensation of vanadium halides is lower than that of the oxides at the second stage; in addition it is seen that curves 1 for vanadium halides have a special characteristic which is hardly perceptible in the case of the oxides; this characteristic is reflected in the definite tendency of successive branches of the curves to be shortened with increasing oxidation stage; this tendency is particularly conspicuous in the case of the large atoms of iodine which appear to hinder one another in their efforts to approach closely to the central atom; such large atoms are therefore compelled in the case of atomic bonds (at high oxidation stages) to make use of more remote and less favorable (possibly even less perturbed) electronic orbits (4d, 4p, 4f instead of 3d), while in the case of ionic bonds (at low oxidation stages) they are compelled to utilize the lower portion of the Coulomb energy of the electrostatic field.

Although we do not claim absolute accuracy for the values listed in Table 1 (data used for vanadium halides [2]), we shall nevertheless attempt to evaluate the order of magnitude of the endo-effect of coordination, i. e., of that reduction in the molecular energy of gaseous molecules that depends on what we might describe as the repulsive influence of atoms arranged coordinatively round a given central atom. For the purpose of rough calculation of this magnitude we take as a measure of the endo-effect of coordination the deviation from additivity which would be expected in the simplest, idealized case if all the subsequent atoms of halogen (after the first) released as much energy as the first atom on combination with the central atom.

TABLE 1

	$\frac{1}{2}V_2O_5$	VF_5	VCl_5	VBr_5	VI_5	TiO_2	TiF_4	$TiCl_4$	$TiBr_4$	TiI_4
Additive value (kcal)	365	670	630	630	610	320	640	520	496	440
True value (kcal)	352	550	390	336	278	318	541	411	372	308
Endo-effect of coordination	13	120	240	294	332	2	99	109	124	132

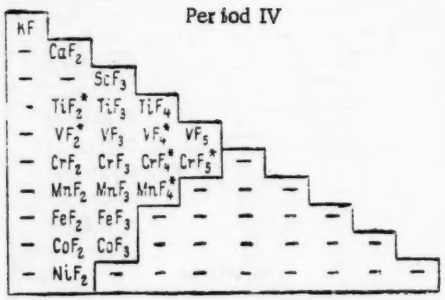
Due to the endo-effect of coordination, the curves 1 in Fig. 1 decrease in steepness with increasing stage of oxidation, i. e., the endo-effect grows with the oxidation stage parallel with the accumulation of coordinated atoms. The transition from relatively small atoms of fluorine to large iodine atoms quickly increases the endo-effect as evident from the tabulated data. Table 2 illustrates how the endo-effect grows with increasing number of coordinated atoms in the case of vanadium (such an increase is noted on comparing Ti with V).

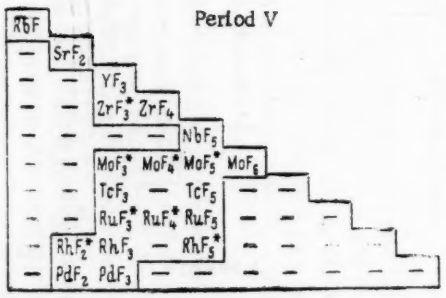
TABLE 2

	Magnitudes of the endo-effect (in kcal with the following numbers of coordinated atoms			
	2	3	4	5
Fluorides	2	10	34	120
Chlorides	24	83	162	240
Bromides	28	120	192	294
Iodides	48	126	211	332

The low magnitude of the endo-effect in oxygen coordination is due partly to the size of the O atom being similar to that of the fluorine atom, as well as,of course,to the ability of the oxygen atom to replace two atoms of fluorine.

Unfortunately, too little is known with certainty about the heats of formation of halides of metals of groups V and VI; moreover, even the data for the thermochemistry of chlorides of molybdenum and tungsten are of doubtful accuracy; no experimental thermochemical characterization of the halides of niobium and tantalum has previously been reported; the thermochemistry of halides of elements of group VIII has also been


Period IV
KF
CaF2
ScF3
TiF2* TiF3 TiF4
VF2* VF3 VF4* VF5
CrF2 CrF3 CrF4* CrF5*
MnF2 MnF3 MnF4*
FeF2 FeF3
CoF2 CoF3
NiF2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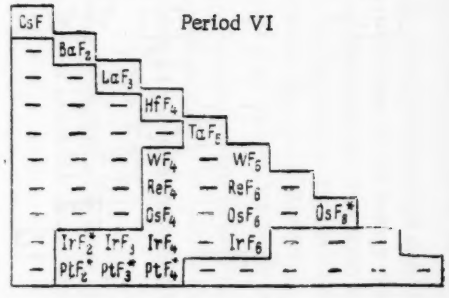
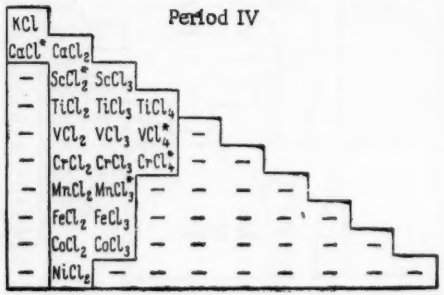
SrF2
YF3
ZrF3* ZrF4
NbF5
MoF3* MoF4* MoF5* MoF6
TcF3 TcF5
RuF3* RuF4* RuF5
RhF2* RhF3 RhF5*
PdF2 PdF3


Period VI
CsF
BaF2
LaF3
HfF4
TaF5
WF4 WF5
ReF4 ReF6
OsF4 OsF6 OsF8*
IrF2* IrF3 IrF4 IrF6
PtF2* PtF3* PtF4*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ScCl2* ScCl3
TiCl2 TiCl3 TiCl4
VCl2 VCl3 VCl4*
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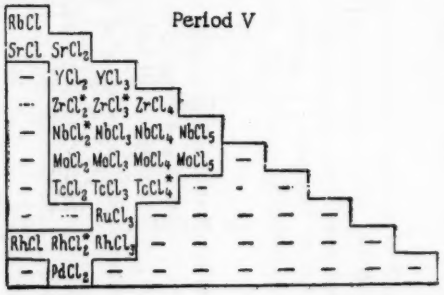
MnCl2 MnCl3*
FeCl2 FeCl3
CoCl2 CoCl3
NiCl2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YCl2 YCl3
ZrCl2* ZrCl3* ZrCl4
NbCl2* NbCl3 NbCl4 NbCl5
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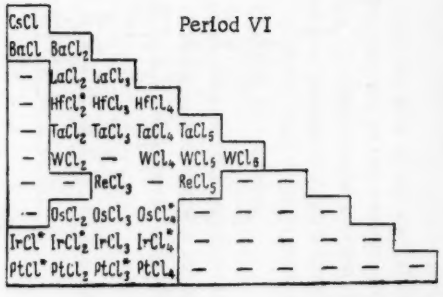
TcCl2 TcCl3 TcCl4*
RuCl3
RhCl RhCl2* RhCl3
PdCl2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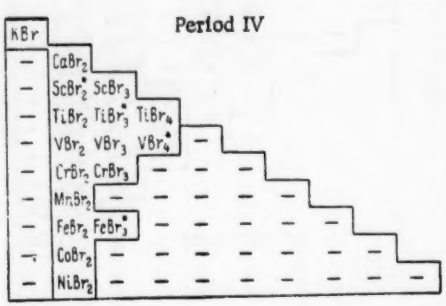
LaCl2 LaCl3
HfCl2* HfCl3 HfCl4
TaCl2 TaCl3 TaCl4 TaCl5
WCl2 WCl4 WCl5 WCl6
ReCl3 ReCl5
OsCl2 OsCl3 OsCl4*
IrCl* IrCl2* IrCl3 IrCl4*
PtCl* PtCl2 PtCl3* PtCl4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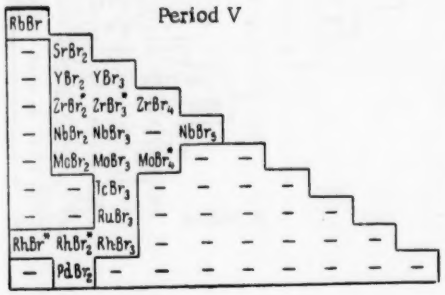
CaBr2
ScBr2* ScBr3
TiBr2 TiBr3* TiBr4
VBr2 VBr3 VBr4*
CrBr2 CrBr3
MnBr2
FeBr2 FeBr3*
CoBr2
NiBr2


Period V
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YBr2 YBr3
ZrBr2* ZrBr3* ZrBr4
NbBr2 NbBr3 — NbBr5
MoBr2 MoBr3 MoBr4*
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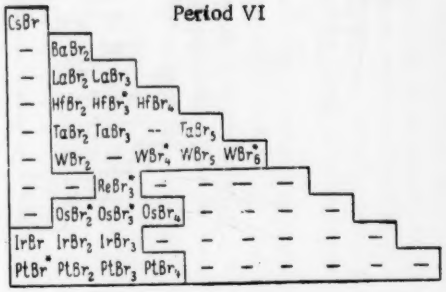
PdBr2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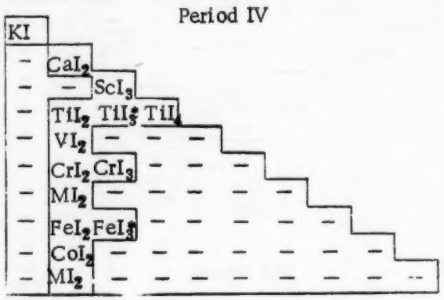
HfBr2 HfBr3* HfBr4
TaBr2 TaBr3 -- TaBr5
WBr2 — WBr4* WBr5 WBr6*
ReBr3*
OsBr2* OsBr3* OsBr4
IrBr IrBr2 IrBr3
PtBr* PtBr2 PtBr3 PtBr4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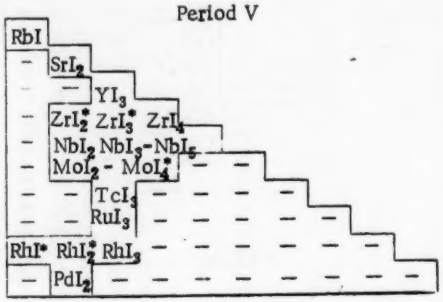
ScI3
TiI2 TiI3* TiI4
VI2
CrI2 CrI3
MnI2
FeI2 FeI3*
CoI2
MnI2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YI3
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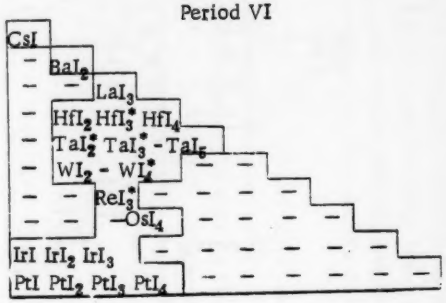
MoI2 - MoI4*
TcI3
RuI3
RhI* RhI2* RhI3
PdI2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BaI2
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TaI2* TaI3* - TaI5
WI2 - WI4*
ReI3*
OsI4
IrI IrI2 IrI3
PtI PtI2 PtI3 PtI4

inadequately studied. In order, therefore, to characterize the role of the endo-effect of coordination, we shall limit ourselves here to listing the hitherto known fluorides, chlorides, bromides and iodides of metals of the even series of the system. The starred items are unstable compounds; the blank spaces correspond to compounds not existing in practice in the free, condensed state and in macroscopic quantities.

These diagrams are self-explanatory and show convincingly that the shift of the upper limit actually depends not only on the over-all slope of the energy curves and the magnitudes of the energy of condensation but also on the endo-effect of coordination. The latter effect increases: 1) from fluorides to iodides; 2) from elements of period VI (with their relatively large atoms) to the elements of period IV (with central atoms of smaller size and increased perturbation energies); 3) from Ca to Ni, from Sr to Pd, from Ba to Pt, once again due to the reduced sizes of the central atom and the increased perturbation energy of its electrons.

Going back to Fig. 1, we cannot fail to note the great difference between the diagrams for the oxides and fluorides of vanadium, which shows that in spite of the proximity of fluorine to oxygen in the system there is a considerable difference between the thermodynamic characteristics of their compounds with the same element (vanadium).

We note the following data on moving along the horizontal row of the system and comparing the nitride, oxide and fluoride of vanadium at the same oxidation stage (the third):

	VN	$^1/_2V_2O_3$	VF_3
$\Delta H_{stand.}$(kcal)	—41	—145	—285

It is clear that there is some general cause not only leading to the great increase in $\Delta H_{stand.}$ on passing from fluoride to oxide, but continuing to take effect on transition from oxide to nitride. We do not yet possess quantitative data for vanadium carbide, but by analogy with other carbides we can assume that the transition from nitride to carbide would also be marked by a large fall in enthalpy of formation. Numerous facts certainly support the theory that the cause of interest to us is generally valid; the data for vanadium may be typical of a whole class of analogous phenomena.

In view of the great interest of an explanation of the above-discussed observations for chemistry (in particular due to the numerous implications of such an explanation) we propose to consider this problem more closely, with special reference to oxides and halides of the alkali and alkaline earth metals. In this case the argument is very considerably simplified since these oxides and halides can be regarded as ionic compounds.

It was clear at the start that the main obstacle to the formation of ionic oxides (and more so of nitrides) is the considerable energy necessary for charging atoms of oxygen and nitrogen with two and three electrons, respectively. The orders of magnitude of this energy are: for O^{-2} +168 kcal; for N^{-3} approximately +700 kcal.

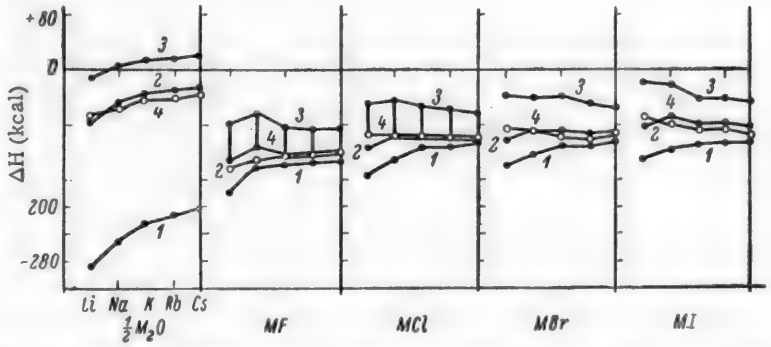

Fig. 2. Energies of formation of oxides and halides of alkali metals (calculated for 1 g-atom of metal). 1) Formation of gaseous molecules from free ions; 2) formation of gaseous molecules from neutral atoms; 3) formation of gaseous molecules from solids; 4) formation of solids from elements.

Due to the high endo-effects of the charge, the over-all exo-balance of the energy of formation of the compounds is sharply reduced, and in the case of nitrides and (especially) carbides the sign may be changed to give an endo-balance. Conversely, the electron affinity of univalent halogen atoms is negative, i. e., the over-all balance $\Delta H_{stand.}$ increases in the case of halides. Data for the energetics of compounds of the alkali metals are plotted in Fig. 2, which shows that the simplest relations exist between curves 1. Curve 1 for the oxides is approximately 1.5 times lower than curve 1 of fluorides, which was to be expected from electrostatic considerations; curves 1 for the fluorides, chlorides, bromides and iodides are arranged one above the other, and this arrangement also has a simple explanation; all of the curves 1 are identical in character, i. e., they rise from the lithium point to the cesium point, as is entirely natural.

TABLE 3

	Energy of transition of electrons from atoms of metals into oxygen or halogen (in kcal)					Note
	Li	Na	K	Rb	Cs	
O	211	202	184	180	174	$I + E_{1/2O^=}$
F	44	35	17	13	7	$I - E_{G^-}$
Cl	40	31	13	7	4	
Br	44	35	17	13	7	
I	55	46	28	24	18	

The most interest is attached to the transition from curves 1 to curves 2, the vertical distances between whose points are equal to the sum of the energies of ionization of the metal and the energy of charging of neutral atoms of O, F, Cl, Br and I.

Since singly-charged halogen ions are formed by exothermic reaction, in practice the addition (allowing for the signs of the effects) of the endo-effect of ionization of the atom of alkali metal to the exo-effect of the charging of the halogen atom results in the case of halides in a small endo-effect; the charging of $^1/_2 O^=$ requires an endo-effect of 84 kcal; together with the endo-effect of the ionization of the atoms of alkali metal, this gives a still higher endo-value (see Table 3).

In the case, therefore, of oxides, curve 2 is very much higher than curve 1, and the rises are small for halides.

Due to the high energies of ionization of atoms of Li and Na, the form of curve 2 in the case of halides differs appreciably from that of curves 1.

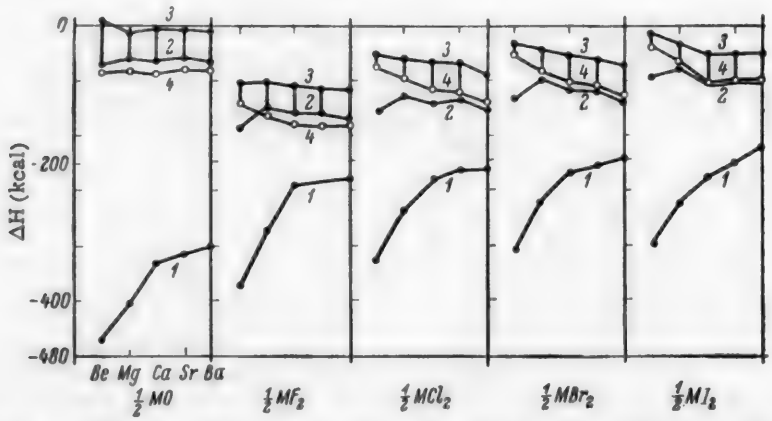

Fig. 3. Energies of formation of oxides and halides of alkaline earth metals (calculated for 1 g-equiv. of metal). 1-3) Formation of gaseous compounds from ions; 4) formation of solids from elements.

Transitions from curves 2 and 3 and subsequently to 4 shift the curves of oxides and halides upwards and then downwards to an equal extent; due to the high energies of sublimation of sodium and, in particular, lithium, and due also to the specific features of the energies of the crystal structures, the curves are again slightly distorted and acquire the standard form familiar to all chemists. We may note that the energies of condensation of oxides of the alkali metals do not greatly differ in order of magnitude from the energies of condensation of halides (especially fluorides).

A different picture is presented by Fig. 3 in which curves 1-4 for compounds of the alkaline earth metals are plotted.

Curves 1, as in Fig. 2, are simple and understandable; the only difference is that the points of the oxides lie not 50% lower than the points of the fluorides but approximately 33%, which is consistent with electrostatic requirements.

The transitions from curves 1 to curves 2 now have a different appearance, since they correspond not to $I_I - E_{G^-}$ or $I_1 + E_{1/2O^=}$, but to $^1/_2 (I_I + I_{II}) - E_{G^-}$ or $^1/E (I_I + I_{II}) + E_{1/2O^=}$; since the half-sum of the first and second ionization potentials is considerably larger than I_I, the rises from curves 1 to curves 2 are here larger than in the case of compounds of the alkali metals, and they are larger not only for oxides but also for halides (Table 4).

TABLE 4

	Energy of transition of electrons from atoms of metals to O or halogen (kcal)					Notes
	Be	Mg	Ca	Sr	Ba	
Oxides	401	345	291	276	259	$^1/_2 I_I + {}^1/_2 I_{II} + E_{1/2O^=}$
Fluorides	233	178	124	109	92	$^1/_2 I_I + {}^1/_2 I_{II} - E_{G^-}$
Chlorides	230	175	121	106	89	
Bromides	233	178	124	109	92	
Iodides	244	189	135	120	103	

Just as in the case of alkali metals, curve 2 for oxides is at a lower level than curves 2 for halides. The transition from 2 to 3 follows the same course as with the alkali metals, but the transition from 3 to 4 (i. e., allowing for the energies of condensation) appreciably changes the picture. Whereas the energies of condensation of halides of the alkali metals only differ insignificantly from the energy of condensation of their oxides, in the case of the alkaline earth metals only the fluorides (but with the exception of BeF_2) have energies of condensation not far from the magnitude of the energies of condensation of the oxides. The energies of condensation rapidly fall off in the order of chlorides, bromides, and iodides; this behavior probably reflects the commencing tendency to pass from purely ionic crystalline structures to molecular structures. The largest fall is noted for Be; it is slightly less for Mg (Table 5).

Owing to the relatively small magnitudes of the energies of condensation, substances like $BeCl_2$, $BeBr_2$, $MgBr_2$, BeI_2, MgI_2 and CaI_2 are formed less exothermically than the corresponding oxides. A comparison of the

TABLE 5

	Energy of condensation in kcal/1 g-equiv [2]									
	Li	Na	K	Rb	Cs	Be	Mg	Ca	Sr	Ba
O	60	55	55	60	60	79	60	69	64	52
F	63	72	52	48	48	30	50	60	55	50
Cl	48	55	51	51	45	17	30	45	46	40
Br	45	49	48	50	46	15	30	40	41	40
I	46	49	44	45	44	14	21	28	35	38

data for $\Delta H_{stand.}$ is plotted in Fig. 4, which contains curves of $\Delta H_{stand.}$ of oxides and halides of elements of groups I and II as well as data for compounds of elements of groups III and IV. We see here a continuation of the process of gradual penetration of the oxides curve into the region of the halide curves, which commences in groups I and II. It is true that in groups III and IV we can no longer make such simple and clear-cut calculations as in the case of the nearly purely ionic compounds of groups I and II, but the experimental values nevertheless reveal a further development of the process of gradual increase of the competing ability of the oxides in relation to the halides; this process is bound up more or less with the higher energies of condensation of the oxides, with the increased volatility of the halides, and with the development of an appreciable endo-effect of coordination which rapidly increases for the halides with increasing number of the group. These aspects are illustrated by Figs. 5 and 6, plotted for compounds of elements of groups III and IV in a similar manner to Figs. 2 and 3.

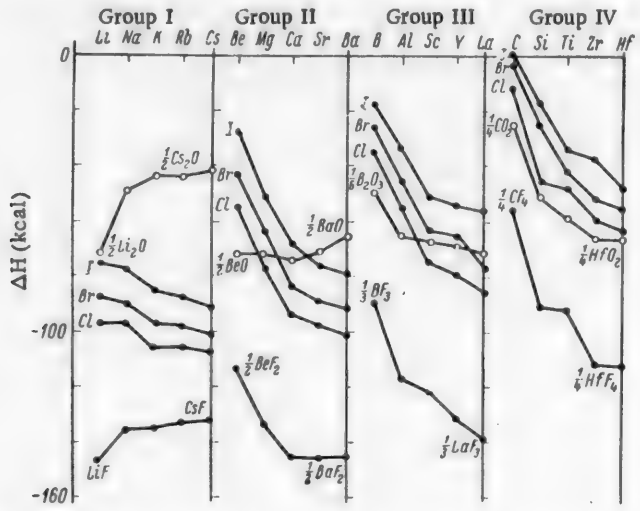

Fig. 4. Standard energies of formation of oxides and halides of elements of groups I to IV of the periodic system (calculated per 1 g-equiv.).

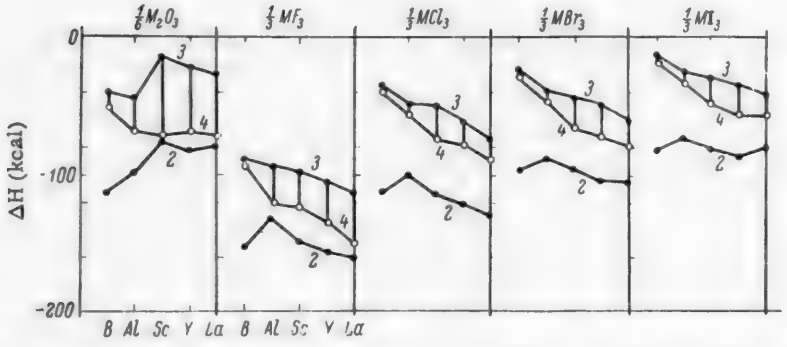

Fig. 5. Energies of formation of oxides and halides of elements of group III (calculated per g-equiv.). 2,3) Formation of gaseous compounds from atoms and elements; 4) the same for standard values.

One of our objectives was to show (as illustrated by Figs. 5 and 6) what an important and even decisive part is played by the enthalpy of condensation of gases and in turn by the properties and structure of the crystals in the chemical characterization of such important classes of compounds as halides and oxides.

In illustration of what has just been said, we again proceed to compare oxides and halides (more specifically chlorides in order to simplify the picture), and we depict the competition of chlorine and oxygen within the framework of the periodic law in the form of graphs corresponding to successive periods of the system (Fig. 7).

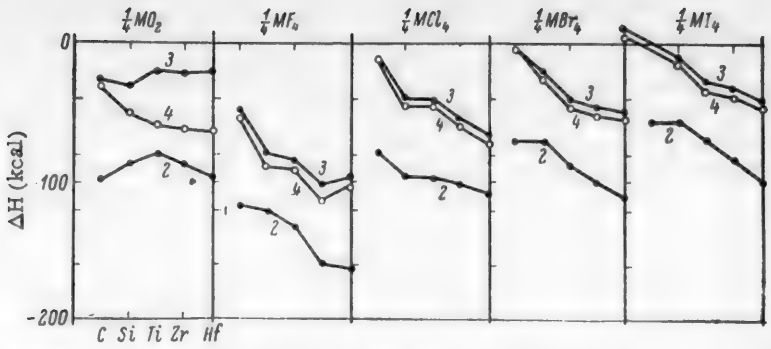

Fig. 6. Energies of formation of oxides and halides of elements of group IV (calculated per g-equiv.). 2,3) Formation of gaseous compounds from atoms and elements; 4) the same for standard values.

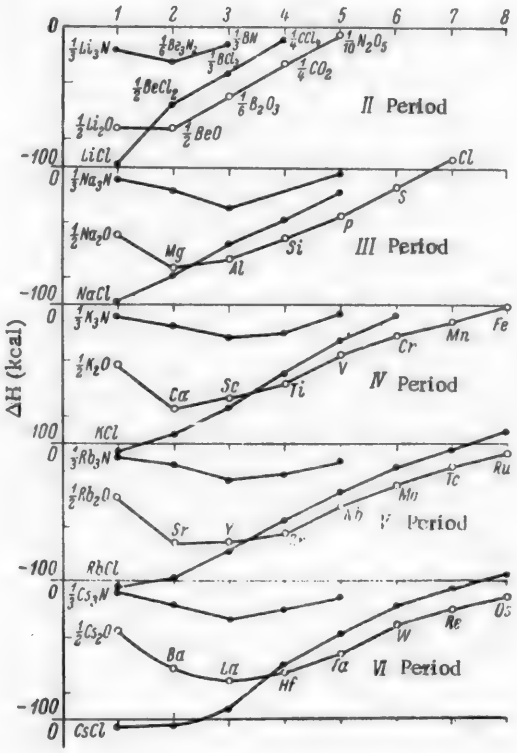

Fig. 7. Standard energies of formation of oxides, chlorides and nitrates (per g-equiv.) for elements of periods II to VI of the periodic system.

We see that in the second period of the system only the point of $^1/_2 Li_2O$ lies appreciably higher than the LiCl point, and therefore lithium oxide must be basic in character and must easily change into the salt LiCl on neutralization. Gaseous HCl acts on $^1/_2 Li_2O$ in such a manner that $^1/_2$ mole of water vapor is formed in place of HCl, and this process is accompanied by a supplementary exo-effect of 7 kcal; it is also easy to calculate the thermal effect in presence of liquid water, when it is necessary to allow for the heat of solution, the energy of condensation of water vapor and the energy of hydration of the oxides.

We already find an opposite picture in the case of beryllium: the energy of formation of a g-equivalent of beryllium oxide exceeds the energy characterizing beryllium chloride; this excess is small, and beryllium oxide is amphoteric and easily hydrolyzed.

Oxides of boron and carbon are weakly acidic: their points lie below the points of the chlorides.

Thus, the most characteristic property of oxides (their basicity or acidity) is revealed by the form, the mutual position and the intersection of the curves of the oxides and chlorides, and this intersection depends in large measure on the energy of condensation of oxides and chlorides. The same intersection also reveals hydrolytic reactions – as the converse of neutralization processes.

In period III the positions of the points of the oxides of Na and Mg endow them with a basic character, while aluminum is seen to be amphoteric, and Si, P, S and Cl are acidic.

The basic properties of Na are more strongly developed than those of Li because the distance between the Na_2O and NaCl points is greater than the distance between the Li_2O and LiCl points. In period IV, apart from K and Ca, Sc also acquires a basic character, as clearly shown in Fig. 7.

In periods V and VI the picture is similar to the diagram for period IV.

In his "Principles of Chemistry" D. I. Mendeleev [3] specially noted that the alkali metals are capable of displacing the alkaline earth metals from their chlorides and that, conversely, the alkaline earth metals displace the alkali metals from their oxides.

These facts are likewise clearly illustrated by Fig. 7. It is easily seen that in the case of chlorides the maximum energy is indeed released by compounds of the alkali metals; on the oxide lines, on the other hand, the point of the oxides of group II elements is at a lower level; the only exception is lanthanum, which releases more energy during oxide formation than does barium. We have included data for nitrides in Fig. 7 in order to further develop and to better explain the views of D. I. Mendeleev; in the case of nitrides the lowest points are in group III – for AlN, ScN, YN and LaN; an exception is BN, which is formed with a lower energy than beryllium nitride.

In all of the three classes of compounds discussed (chlorides, oxides and nitrides) the minimum points on the energy curves thus correspond to formulas of the type of AB (NaCl, MgO, AlN).

D. I. Mendeleev attached importance to this relation and indicated the simplicity of the formula in the course of an attempt at explanation.

We now see that this truly noteworthy circumstance, which confirms to some extent Dalton's hypothesis of the existence of a principle of maximum simplicity for the formulas of the most probable chemical compounds, is based on the energy concept. The absence of an endo-effect of coordination for molecules MX, the low energy of ionization of atoms of the alkali metals, the negligible energy of dissociation into atoms of these metals, and the quite high energy of condensation of molecules MX capable of building up into a purely ionic lattice all help to account for the exceptional stability of compounds of alkali metals with chlorine.

In the case of oxides we are dealing with exceptionally stable substances with considerable energies of condensation, and for this it is desirable to have an ionic crystal structure. The $O^{=}$ anion, however, is itself unstable since it is formed endothermically, and M^{+} cation of not very large size (Li^{+} is preferable to Na^{+} and K^{+}) are suitable for its stabilization; better still are M^{++} ions, and this fact accounts for the exceptional stability of the oxides of the alkaline earth metals. Still more highly charged cations of the type of M^{+++} require too much energy for their formation, especially since molecules of the type of M_2O_3 no longer have a purely ionic structure and release less energy per g-equiv than the MO molecule.

Although ionic oxides of the type of M_2O and MO can consequently be formed and can be stable, especially in the solid state, their energies of formation are nevertheless somewhat lowered due to the endo-effect of $O^{=}$ formation, and for this reason these oxides have a basic character, i. e., they are exothermically transformed into chlorides and in general behave as if they had remained in the inviolable form of M^{+} and M^{++} cations after having got rid of the energetically unfavorable $O^{=}$ anion; this can be achieved by various methods, leading either to disappearance of the free negative charges or to reduction in their number, or (what is especially interesting and important) to their dissipation, scattering or spread (i. e., to distribution of two charges over any two different atoms). Such are, for example, the following processes of dissipation of electrons.

$$Ca^{++}O^{=} + H_2O = Ca^{++}(OH^{-})_2$$
$$Ca^{++}O^{=} + 2HCl = Ca^{++}(Cl^{-})_2 + H_2O$$
$$Ca^{++}O^{=} + 3C = CO + Ca^{++}(^{-}C{-}C^{-})$$
$$Ca^{++}O^{=} + SO_3 = Ca^{++}(SO_4^{=})$$
$$Ca^{++}O^{=} + CO_2 = Ca^{++}(CO_3^{=})$$

In the last three examples doubly-charged anions are formed whose negative charges are spread, since they are not attached to the same atom. Multi-charged and at the same polyatomic anions are also encountered extremely rarely in the free state (in a gaseous discharge), which affords evidence of their poor stability or even of their complete instability; at the same their existence is more probable than that of monoatomic ions of $O^{=}$, $N^{=}$, etc. Stabilization of polyatomic anions in crystals and in solutions evidently proceeds with very much greater facility than the stabilization of monoatomic ions.

Characteristic of the simplest nitrides of an ionic nature is the presence of the $N^{\equiv}$ anion, which is even more unstable than the $O^{=}$ anion. Due to the very large endo-effect of formation of $N^{\equiv}$, its stabilization is

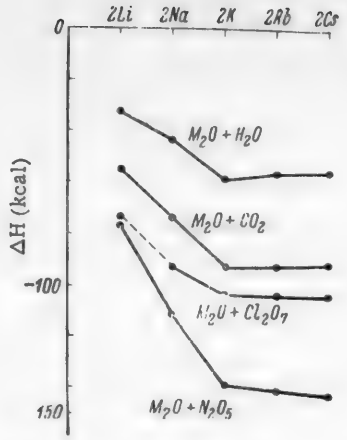

Fig. 8. Energy of combination of oxides of the alkali metals with water and acidic oxides.

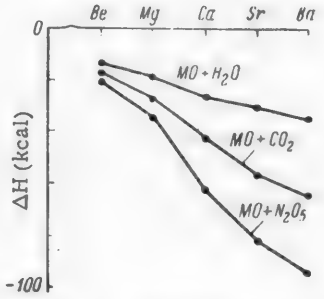

Fig. 9. Energies of combination of oxides of the alkaline earth metals with water and acid anhydrides.

better effected with the help of the relatively small cations of Li^+ and Be^{++}, but even more suitable are the cations of Al^{+++}, Sc^{+++}, etc. For this reason the most stable nitrides are actually found in group III of the system. In addition, due to the presence of the unstable $N^{\equiv}$, nitrides are still less exothermic than oxides, and ΔH curves of their formation fall in Fig. 7 into a region not far from the zero line.

Following out this line of reasoning, it is easy to see that the ionic carbides must lie at a still higher level and must enter the endo-region. In order to avoid the energetically very unfavorable $C^{\equiv}$ ions, the compound is transformed into atomic (nonionic), crystalline structures of the diamond type (case of SiC) or proceeds to lose its negative charges by dissipation with formation of diatomic anions, of the type of $^{-}C \equiv C^{-}$ for example, and gives rise to the acetylides of lithium and calcium which still appear in the exo-region but higher than the nitrides.

In the foregoing discussion we referred to the principle of dissipation of negative charges, i. e., to the tendency of these charges not to remain at one atom only. It is well known, of course, that multi-charged cations are likewise formed with difficulty, but in chemistry we have many examples, nevertheless, of fully stable, doubly-charged and at the same time monoatomic cations; we also encounter triply-charged cations and even occasionally quadruply-charged ones. There is a dissymmetry in the ratio of anions to cations: the multiply-charged anions that we know to be stabilized by the energy of crystallization and solvation are predominantly only monoatomic, i. e., with charges shared between different atoms, for example, $SO_4^{=}$, $CO_3^{=}$, etc.; $O^{=}$, $S^{=}$ and $N^{\equiv}$ ions are developed in exceptional cases by especially firm stabilization by their partners and always strive to disappear by transformation into other substances. Polyatomic anions are therefore encountered in compounds more frequently than polyatomic cations.

We shall now present some characteristic cases of dissipation reactions of negative charges. The most important of these are transformations of oxides of the alkali and alkaline earth metals into peroxides, superoxides and ozonides. All of these cases involve an exothermic reaction which is accompanied by dissipation of the electrons due to formation of coordinated bonds.

$$\begin{matrix} K^+ \\ K^+ \end{matrix} O^{=} + {}^1/_2O_2 = \begin{matrix} K^+ \\ K^+ \end{matrix} (O^{-}—O^{-})$$

$$\begin{matrix} K^+ \\ K^- \end{matrix} O^{=} + {}^3/_2O_2 = K^+(^{-}O—O) + K^+(O^{-}—O)$$

Compounds such as BeO and Li_2O are the least readily transformed into peroxides since the $O^{=}$ ions are stabilized in them by small cations.

A similar case was discovered in our laboratory by S. M. Arria [4] who succeeded in synthesizing barium pernitride, i. e., in realizing the dissipation of the charges of the nitrogen anion; this compound has the formula BaN_2 or Ba^{++} ($^{-}N=N^{-}$) and is an analog of BaO_2 in a certain sense.

Still more interesting as examples of electron dissipation processes are reactions in which hydrates of basic oxides and salts are formed, i. e., the process of combination of two oxides. The exothermic effects of such pro-

cesses, in which the energetically unfavorable $O^=$ anions disappear, are plotted in Figs. 8 and 9 for the simplest compounds of the alkali and alkaline earth metals.

We see that in these cases the carbonates are formed from the oxides with greater liberation of energy than the basic hydrates of the oxides, and therefore CO_2 will neutralize the latter; the exothermic effect of formation of nitrates is even greater than that of the formation of carbonates, and therefore nitrogen pentoxide will displace CO_2 from carbonates. But it is still more characteristic that processes of combination of an ionic, basic oxide with water and acid anhydrides are exothermic and accompanied by dissipation of electrons.

Analogous examples could also be adduced for sulfides, the $S^=$ ion of which is capable of giving polyions with added atoms of sulfur, or hydrosulfide anions and polyatomic anions during oxidation (for example, on passing from Na_2S to Na_2SO_4) or on combination of basic sulfides with acids.

We have compared the ΔH of formation of higher oxides and chlorides in the horizontal series of the periodic system. We obtain a similar picture if we compare the oxides and chlorides of a given element at different oxidation stages. In this case again, at the lower oxidation stages the ΔH of formation of chlorides will exceed the ΔH of formation of the oxides, while at the higher stages the opposite law holds good. As an example, we present data for titanium compounds.

	TiO	$^1/_2$ Ti_2O_3	TiO_2
ΔH (kcal)	—122	—181.5	—225.6
	$TiCl_2$	$TiCl_3$	$TiCl_4$
ΔH (kcal)	—124	—172	—196
Δ	—2	~10	~30

From the foregoing considerations we arrive logically at the well-known law that the acidity or basicity of an oxide is governed not only by the chemical nature of the oxidized element but also to a considerable extent by the degree of oxidation. Both manganese (a typical cationogen in the lower oxidation stages) and chlorine (an element characterized by a great electron affinity in the seventh oxidation stage) give rise to typical acidic oxides.

SUMMARY

1. An oxide may be characterized as a base by the amount by which the enthalpy of formation of the chloride of the same metal exceeds the enthalpy of formation of the oxide (at the same oxidation stage).

When the enthalpy of formation of an oxide considerably exceeds the enthalpy of formation of the corresponding chloride, the latter is susceptible to hydrolysis and can be characterized as an acid chloride, while the oxide itself will be acidic. When the enthalpies of formation of chloride and oxide are very similar, the oxide is amphoteric.

2. In the case of a metal capable of forming a series of oxides, the curves of $\Delta H_{stand.}$ versus oxidation stage (calculated on 1 g-atom of metal) are so arranged that the curve of the chlorides is at the lower oxidation stages below the curve of the basic oxides; after intersection of the curves (at the amphoteric oxide) the curve of the chlorides for high oxidation stages moves above the curve of the oxides. This law can be utilized for evaluation of the enthalpy of formation of oxides and chlorides for which few data are available.

3. On plotting the curves of enthalpies of formation (calculated per g-atom of oxidized element) of higher oxides and chlorides of elements in the same series of the periodic system, we observe intersection of the curves. Due to this intersection, the oxides TiO_2, V_2O_5, CrO_3 and Mn_2O_7 are acidic; the acidity of Mn_2O_7 is accordingly associated with the ability of Mn to give an oxide at a high (seventh) oxidation stage.

4. The relative position of the curves which has just been mentioned is not solely associated with the energies of the interatomic bonds; it also depends: a) on the endo-effect of formation of $O^=$ ions, which decreases the enthalpy of formation of basic (lower) oxides; b) on the endo-effect of coordination of the atoms of chlorine round the central atom which lowers the enthalpy of formation of the higher chlorides; c) on the fall in the exo-effect of the energy of condensation of gaseous compounds in the case of chlorides with increasing stage of oxidation which is very much faster than in the case of oxides.

5. Neutralization of basic oxides by acid anhydrides (CO_2, N_2O_5) depends on the tendency of the electrons to dissipate, i. e., not to accumulate at one atom ($O^=$, $N^=$, etc.) but to spread themselves over different atoms of a monatomic anion, which is energetically favorable. The same cause (the unprofitableness of accumulation of negative charges at one atom) results in the enthalpy of formation falling in the order of chlorides, oxides, nitrides and carbides.

6. An explanation is given of D. I. Mendeleev's observation of the tendency of elements to form particularly stable compounds in formation of substances with the formula AB.

7. It was noted that the endo-effect of coordination increases: a) from fluorides to iodides; b) from elements of period VI to elements of period IV; c) from Ca to Ni, from Sr to Pd and from Ba to Pt.

8. The endo-effect of coordination of oxygen atoms is considerably lower than for fluorine atoms.

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THE DISSOCIATION CONSTANTS OF TRIHYDROXYGLUTARIC ACID

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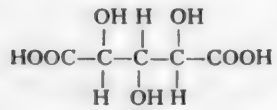
Hydroxycarboxylic acids and their compounds with metals have recently attracted an increasing amount of attention due to the importance which they are acquiring in science and technology. At the same time very little work has been done on the physicochemical properties of these acids, and any work at all in this field has been concentrated on a small number of hydroxyacids. Tartaric acid is the member of the hydroxydicarboxylic acid series that has attracted most attention. Trihydroxyglutaric acid differs from tartaric acid in containing one more $H-\overset{|}{\underset{|}{C}}-OH$ group. Its physicochemical properties have scarcely been studied. A number of investigations have indicated, however, the possibility of obtaining cheap trihydroxyglutaric acid and of employing it in place of tartaric and citric acids.

The purpose of the present work is to determine the first and second acid dissociation constants of optically active xylotrihydroxyglutaric acid* (A) with the help of potentiometric titration.

The first acid dissociation constant of xylotrihydroxyglutaric acid was calculated by Ruff [1] on the basis of the electrical conductivity of its solutions. At 25° it was found equal to $6.6 \cdot 10^{-4}$. There are no data for the second acid dissociation constant in the literature.



(A)

Materials. For the preparation of solutions we started from previously purified commerical trihydroxyglutaric acid, made at the pilot plant of the Fergana wood hydrolysis works, which before purification contained 99% of trihydroxyglutaric acid.** To the hot, concentrated solution of this trihydroxyglutaric acid was added active carbon for decoloration of the solution) and pulverized BaS in small portions until the filtered solution no longer gave a reaction for the SO_4^{2-} ion. The solution was filtered, concentrated on a water bath and rapidly cooled. The acid separated in finely crystalline form and was isolated from the mother liquor and recrystallized from aqueous solution. The acid was washed on the filter with a little water and then with ethyl alcohol, and was dried at first in the air and then in a desiccator over sulfuric acid. The so purified trihydroxyglutaric acid had m. p. 134°.

Solutions of trihydroxyglutaric acid were made up by weight. The NaOH solution used for titration was free of CO_2 and was prepared by the procedure of Kolthoff and Sandell [2].

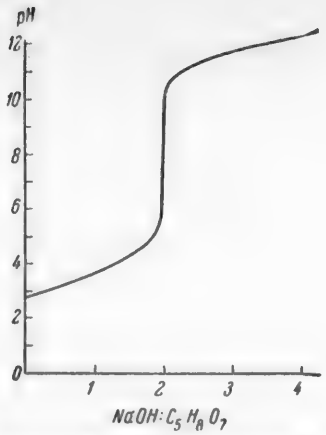
Apparatus. The "Orion" pH-meter (type 2512 with a glass electrode) was used for measurements of pH. The comparison electrode was a saturated calomel electrode.

The temperatures of the solutions were kept constant to within 0.1° in a thermostat.

Results of potentiometric titration of a 0.005 M solution of trihydroxyglutaric acid with alkali at 20° are plotted in the diagram. In the measurements 40 ml of acid of the above concentration was titrated with 0.1045 N NaOH solution. In the diagram the pH value is plotted against the number of equivalents of alkali added per mole of acid present in the original solution.

* In the further course of this paper xylotrihydroxyglutaric acid will be called simply trihydroxyglutaric acid.

** We obtained this acid from the All-Union Institute of Research of the Hydrolysis and Sulfite Cellulose Industry.



Titration of trihydroxyglutaric acid.

The titration curve does not exhibit a potential jump corresponding to the neutralization of the first hydrogen ion. The inflection on the titration curve corresponds to the addition of two equivalents of alkali per mole of acid. This testifies to the closeness between the values of the first and second dissociation constants.

The pH of the neutral solution, found from the titration curve, is 7.8. The titration curve does not indicate the removal of hydrogens from the alcohol groups on further addition of alkali to a pH of ~ 12.

Due to the close similarity between the values of K_1 and K_2, the calculation of K_1 from the formula pH = $= {}^1/_2\ pK_1 + {}^1/_2 \log C_K$ may be seriously in error. Calculation of K_2 from the pH of the acid salt may also include a serious error due both to the entry of K_1 into the formula and to the similarity between K_1 and C_K [3]. We therefore made use of the system of equations based on the law of mass action for calculation of the constants of acid dissociation of trihydroxyglutaric acid.

Different mathematical variants are known of this method which is used for calculation of the dissociation constants of polybasic acids and of the instability constants of their compounds with metals [3-6]. We made use of the algebraic variant of the method described by Martell and Calvin [6] when they calculated the dissociation constants of ethylenediamine tetraacetic acid.

We use the following symbols: $\underline{a}$ is the number of equivalents of alkali used up in the titration; $[TpH_2]$ is the concentration of undissociated trihydroxyglutaric acid, $[TpH^-]$ is the concentration of anions of the monosubstituted sodium salt, $[Tp^{2-}]$ is the concentration of anions of the disubstituted sodium salt, $[H^+]$ is the hydrogen ion concentration, C_K is the total molar concentration of all of the forms of the acid (ionic and molecular).

The following equation will be valid for all of the points of the potentiometric titration curve with $\underline{a} < 2$:

$$[TpH_2] + [TpH^-] + [Tp^{2-}] = C_k \qquad (1)$$

It follows from the requirement of electrical neutrality of the solution that:

$$aC_k + [H^+] = [TpH^-] + [Tp^{2-}], \qquad (2)$$

since the concentration of $[Na^+]$ ions = aC_K.

Results of Calculation of the Dissociation Constants of Trihydroxyglutaric Acid at 20° ($C_K = 5 \cdot 10^{-3}$)

No. of point	a	pH	$[H^+]$	$K_1 \cdot 10^4$	$K_2 \cdot 10^6$
1	0.3135	3.02	$9.56 \cdot 10^{-4}$	8.3	6.8
	1.2540	4.01	$9.78 \cdot 10^{-8}$		
2	0.5225	3.21	$6.16 \cdot 10^{-4}$	8.1	6.1
	1.1495	3.87	$1.35 \cdot 10^{-4}$		
3	0.4180	3.11	$7.77 \cdot 10^{-4}$	8.3	5.8
	1.0450	3.76	$1.74 \cdot 10^{-4}$		
4	0.2090	2.93	$1.17 \cdot 10^{-3}$	8.3	5.0
	0.9405	3.65	$2.24 \cdot 10^{-4}$		
5	0.6270	3.29	$5.13 \cdot 10^{-4}$	8.8	6.9
	1.4630	4.30	$5.01 \cdot 10^{-5}$		
	Mean value	. . . . .		8.4	6.1

From the equation of the first dissociation stage:

$$TpH_2 \rightleftarrows H^+ + TpH^-$$

we have:

$$K_1 = \frac{[H^+][TpH^-]}{[TpH_2]} \quad (3)$$

From the equation of the second dissociation stage:

$$TpH^- \rightleftarrows Tp^{2-} + H^+$$

we have:

$$K_2 = \frac{[H^+][Tp^{2-}]}{[TpH^-]} \quad (4)$$

On solving the system of four equations (1)-(4) for K_1 and K_2 and eliminating the unknowns $[TpH_2]$, $[TpH^-]$ and $[Tp^{2-}]$, we obtain:

$$K_2\left\{\frac{(2-a)\,C_x}{[H^+]} - 1\right\} - \frac{1}{K_1}[H^+]\,(aC_x + [H^+]) = (a-1)\,C_x + [H^+] \quad (5)$$

On inserting the values of $[H^+]$ calculated from potentiometric titration data when $a < 2$, we obtain a series of pairs of equations with two unknowns, K_1 and K_2. By solving these equations we obtain the values of both of the constants.

The table contains the results of calculations for five pairs of points. The calculations were actually carried out for a larger number of points of the titration curve; the deviations of the results from the mean lie within the same limits as those presented in the table.

SUMMARY

The dissociation constants of xylotrihydroxyglutaric acid at 20° were calculated from potentiometric titration data. The values obtained were $K_1 = 8.4 \cdot 10^{-4}$; $K_2 = 6.1 \cdot 10^{-5}$.

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PHYSICOCHEMICAL INVESTIGATION OF THE INTERACTION OF ACETONE WITH ACETIC ACID AND ITS DERIVATIVES

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Previous papers [1-4] described investigations of the reaction of urea with acetic acid and its derivatives. It was established that chemical reaction in the system is intensified with increasing substitution of chlorine for the hydrogen atoms in the acetic acid radical. A similar trend was observed in systems of acetamide with acetic acid and its chloro-derivatives [5-8]. It was found that replacement of one amino group in urea by a methyl group leads to still greater intensification of chemical interaction, which is reflected to a large extent in the composition-property diagrams and in the isotherms of electrical conductivity, viscosity, surface tension and density.

TABLE 1

Density (d) and Viscosity (η) in the System Acetone–Acetic Acid

CH_3COOH mole%	0°		20°		30°	
	d	η	d	η	d	η
0	—	—	0.806	0.44	0.791	0.39
10	0.849	0.57	0.835	0.50	0.819	0.44
20	0.874	0.66	0.858	0.56	0.845	0.49
30.2	0.900	0.77	0.883	0.62	0.870	0.53
39.8	0.921	0.87	0.905	0.69	0.896	0.60
50.1	0.950	1.01	0.930	0.79	0.918	0.67
60.3	0.973	1.17	0.954	0.89	0.949	0.75
69.8	0.997	1.33	0.981	0.99	0.972	0.84
80.0	1.022	1.50	1.006	1.10	0.999	0.90
89.8	1.047	1.63	1.033	1.19	1.025	0.96
94.9	1.060	1.69	—	—	—	—
100	1.075	1.73	1.057	1.25	1.053	1.053

TABLE 2

Surface Tension in the System Acetone–Acetic Acid

CH_3COOH mole%	0°	20°	30°
0	—	24.43	23.29
10	27.34	25.12	24.15
20	27.88	25.74	24.84
30	28.33	26.32	25.45
40	28.70	26.85	26.05
50	29.05	27.25	26.45
60	29.35	27.52	26.73
70	29.60	27.72	26.85
80	29.75	27.87	27.00
90	29.75	27.85	27.00
100	29.70	27.74	26.90

TABLE 3

Density (d), Viscosity (η) and Surface Tension (σ) in the System Acetone–Monochloroacetic Acid

$CH_2ClCOOH$ mole%	20°			30°			40°		
	d	η	σ	d	η	σ	d	η	σ
0	0.806	0.44	24.43	0.791	0.39	23.29	0.786	0.35	21.95
10	0.864	0.55	25.84	0.860	0.48	24.83	0.853	0.48	23.60
20	0.935	0.70	27.55	0.924	0.61	26.64	0.917	0.52	25.31
30	0.999	0.92	29.35	0.982	0.77	28.45	0.975	0.65	26.90
40	1.060	1.21	31.40	1.053	0.99	30.40	1.042	0.83	28.80
50	1.126	1.68	33.31	1.117	1.33	32.13	1.105	1.05	30.64
60	1.184	2.16	35.32	1.180	1.76	34.05	1.166	1.38	32.35
70	—	—	—	—	—	—	1.234	1.85	34.07

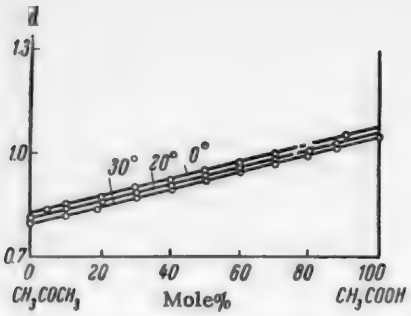

Fig. 1. Density in the system acetone–acetic acid.

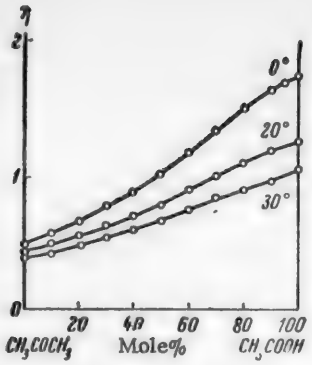

Fig. 2. Viscosity in the system acetone–acetic acid.

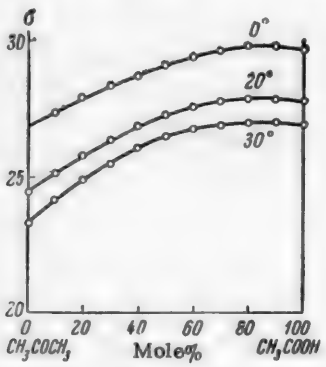

Fig. 3. Surface tension in the system acetone–acetic acid.

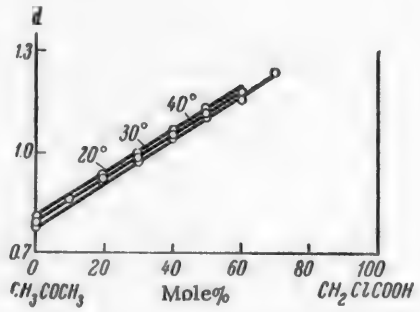

Fig. 4. Density in the system acetone–monochloroacetic acid.

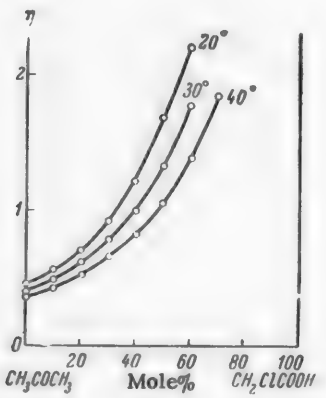

Fig. 5. Viscosity in the system acetone–monochloroacetic acid.

It appeared of interest to study the character of the interaction of acetone with acetic acid and its chloroderivatives in order to check the validity of the theoretical assumptions made previously [6] about the nature of the chemical bond in systems consisting of urea and acetamide on the one hand and acetic acid and its chloroderivatives on the other, and involving the presence of a hydrogen bond.

In the present paper we present the results of investigation of three binary systems: acetone–acetic acid, acetone–monochloroacetic acid, and acetone–trichloroacetic acid.* The viscosity, density and surface tension were studied. We described the experimental procedure previously [2, 5, 9].

Concentrations were expressed in molar percentages, viscosities in centipoises, and surface tensions in dynes/cm. The starting substances were purified: acetone by three redistillations, acetic acid by freezing, trichloroacetic acid by distillation.

The literature does not contain any data for the fusibility of the systems acetone–acetic acid (or its chloroderivatives). In our laboratory we likewise failed to obtain fusibility data.

* E. G. Veselkova participated in the experimental work.

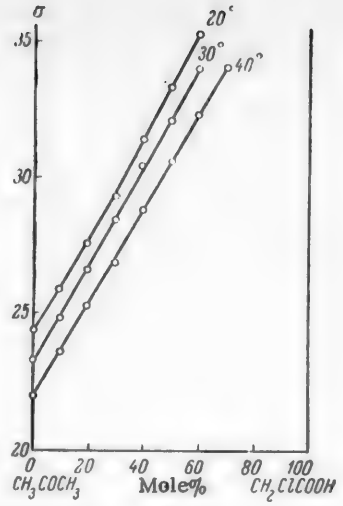

Fig. 6. Surface tension in the system acetone–monochloroacetic acid.

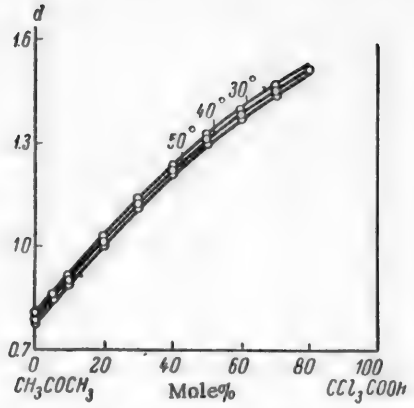

Fig. 7. Density in the system acetone–trichloroacetic acid.

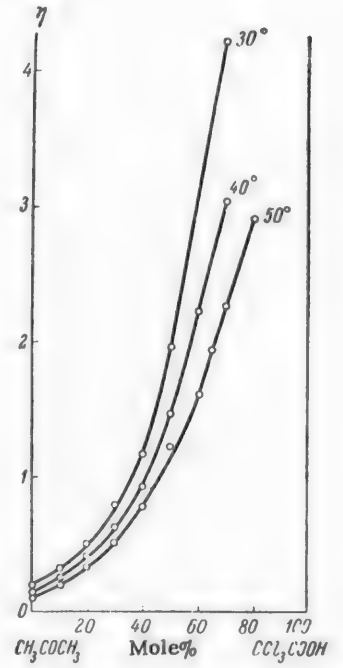

Fig. 8. Viscosity in the system acetone–trichloroacetic acid.

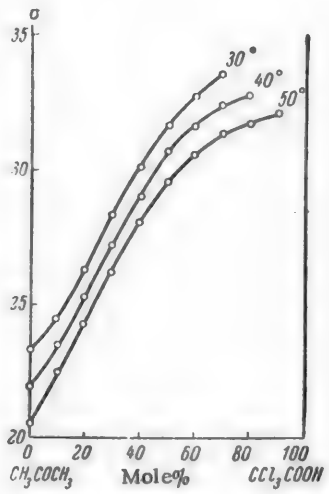

Fig. 9. Surface tension in the system acetone–trichloroacetic acid.

We studied the system acetone–acetic acid in the liquid phase on the basis of data for density, viscosity and surface tension at 0, 20 and 30° (Figs. 1-3; Tables 1 and 2).

The system acetone–monochloroacetic acid was studied in the liquid phase on the basis of data for density, viscosity and surface tension at 20, 30 and 40° (Figs. 4-6; Table 3).

In the case of the system acetone–trichloroacetic acid, the density, viscosity and surface tension were studied at 30, 40 and 50° (Figs. 7-9; Table 4).

TABLE 4

Density (d), Viscosity (η) and Surface Tension (σ) in the System Acetone–Trichloroacetic Acid

CCl_3COOH (mole%)	30°			40°			50°		
	d	η	σ	d	η	σ	d	η	σ
0	0.791	0.39	23.29	0.786	0.35	21.95	0.771	0.31	20.60
10	0.915	0.52	24.45	0.899	0.45	23.43	0.889	0.40	22.44
20	1.030	0.71	26.22	1.017	0.61	25.27	1.010	0.53	24.25
30	1.137	0.99	28.27	1.125	0.83	27.18	1.118	0.71	26.15
40	1.234	1.37	30.00	1.225	1.12	28.90	1.220	0.99	28.00
50	1.331	2.16	31.60	1.320	1.67	30.71	1.309	1.42	29.52
60	1.408	—	32.71	1.393	2.43	31.65	1.374	1.81	30 55
70	1.477	4.42	33.50	1.465	3.23	32.31	1.453	2.47	31.29
80	—	—	—	—	—	32.70	1.523	3.10	31.67
90	—	—	—	—	—	—	—	—	31.99

DISCUSSION OF RESULTS

The viscosity isotherms of the system acetone–acetic acid are S-shaped. This points to the existence of a compound in the fused homogeneous medium with the composition $2CH_3COOH \cdot CH_3COCH_3$. The decreasing steepness of the curve with rising temperature is due to the dissociation of the compound in the melt. The convexity of the surface tension isotherm is also a sign of the presence of a compound in the homogeneous medium. The maximum bulge corresponds to a 2:1 compound.

In the system acetone–monochloroacetic acid the viscosity isotherms are concave, possibly due to dissociation of an associated component and the formation of a compound. The character of the viscosity isotherms resembles that of the viscosity isotherms in the system urea–monochloroacetic acid. It may be thought that two compounds are likewise formed in the system acetone–monochloroacetic acid: $CH_3COCH_3 \cdot CH_2ClCOOH$ and $CH_3COCH_3 \cdot 2CH_2ClCOOH$. The surface tension alters smoothly with increasing content of monochloroacetic acid, and the isotherms are free of characteristic discontinuities that might have been associated with the formation of compounds in the homogeneous fused phase. However, the shape of the surface tension isotherms of this system is reminiscent of that of the surface tension isotherms of the system urea–monochloroacetic acid in which other methods revealed the occurrence of chemical interaction.

In the system acetone–trichloroacetic acid the density isotherms are convex; this indicates a slight contraction associated with chemical interaction of the components in the system and with formation of the compound $CH_3COCH_3 \cdot CCl_3COOH$. The convexity of the surface tension isotherms also indicates the existence of a 1:1 compound. As in the case of the system acetone–monochloroacetic acid, the viscosity isotherms are concave, thus reflecting the dissociation of an associated component and the formation of a compound.

Comparison of the data for the three systems shows that acetone on the one hand and acetic acid and its chloro-derivatives on the other hand in the liquid phase form binary compounds whose stability increases slightly with increasing replacement of hydrogen by chlorine in the acetic acid radical. This characteristic is particularly reflected on the curves of density and surface tension. In the latter the degree of curvature increases on passing from the system acetone–acetic acid to the system acetone–trichloroacetic acid. It should be noted that of the three components – urea, acetamide and acetone – acetamide reacts more vigorously than the others with acetic acid and its chloro-derivatives, due to its higher dielectric constant (acetamide has a constant of 59.10, and acetone one of 21.45). Therefore when organic acids dissolve in acetamide, the degree of dissociation with cleavage of a hydrogen ion is greater. This facilitates the formation of more stable compounds of acetamide with acetic acid and its chloro-derivatives [10].

SUMMARY

1. The systems acetone–acetic acid, acetone–monochloroacetic acid and acetone–trichloroacetic acid were investigated by the methods of measurement of density, viscosity and surface tension.

2. In a homogeneous fused medium, the system acetone–acetic acid contains the compound $2CH_3COOH \cdot CH_3COCH_3$, while the system acetone–trichloroacetic acid contains the compound $CCl_3COOH \cdot CH_3COCH_3$. It is suggested that the system acetone–monochloroacetic acid contains the compounds

$$CH_2ClCOOH \cdot CH_3COCH_3 \text{ and } 2CH_2ClCOOH \cdot CH_3COCH_3.$$

3. Interaction of the components in the systems acetone–acetic acid and its chloro-derivatives increases with increasing replacement of hydrogen by chlorine in the acetic acid radical.

4. Examination of the isotherms of density, viscosity and surface tension in the systems of urea, acetamide and acetone with acetic acid and its derivatives leads to the conclusion that the chemical processes taking place in these systems are all associated with the presence of a hydrogen bond.

5. The stabilities of the compounds formed in the systems urea–, acetamide– and acetone–acetic acid (and its chloro-derivatives) are compared. The most stable compounds in a homogeneous medium are compounds of acetamide with acetic acid and its chloro-derivatives, since acetamide has the highest dielectric constant.

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INVESTIGATION OF THE INTERACTION OF DIPHENYLAMINE WITH ORGANIC ACIDS BY THE METHODS OF PHYSICOCHEMICAL ANALYSIS

N. K. Tsvetkova and D. E. Dionis'ev*

Aromatic amines are more weakly basic than aliphatic amines, since the electronegative benzene ring lowers the basicity of an aromatic amine. Especially strongly depressed are the basic properties of secondary, purely aromatic amines such as diphenylamine which contains two benzene rings. It was therefore of interest to study the nature of the interaction of diphenylamine with substances possessing acidic properties, i. e., organic acids.

Equimolar compounds are formed by diphenylamine with hydrochloric, hydrobromic and sulfuric acids: $C_{12}H_{11}N \cdot HCl$, $C_{12}H_{11}N \cdot HBr$, $C_{12}H_{11}N \cdot H_2SO_4$. With hydrofluoric acid it gives two compounds: $C_{12}H_{11}N \cdot 2HF$ and $C_{12}H_{11}N \cdot 3HF$. With nitric acid the compounds $4C_{12}H_{11}N \cdot HNO_3$ and $3C_{12}H_{11}N \cdot 2HNO_3$ were isolated.

The following compounds of diphenylamine with aliphatic acids are known: a compound of diphenylamine with lauric acid $C_{12}H_{11}N \cdot C_{11}H_{23}COOH$ detected by O. A. Osipov and N. A. Trifonov [1] by the methods of physicochemical analysis; a compound of diphenylamine with oxalic acid $C_{12}H_{11}N \cdot C_2H_2O_4$ [2] and a stable, thermally undissociatable compound of diphenylamine with maleic acid $C_{12}H_{11}N \cdot C_4H_2O_3$, obtained by O. A. Osipov and Iu. V. Fedorov [3].

EXPERIMENTAL

Experimental procedure. Diphenylamine was recrystallized 3 times from ligroine and dried in a desiccator in a stream of warm air. The purified product had m. p. 53°. Monochloroacetic acid was purified by distillation and had m. p. 63° and b. p. 186.5°. Trichloroacetic acid (chemically pure grade) was redistilled 3 times and kept in sealed ampoules; m. p. 59° and b. p. 197°. p-Nitrobenzoic acid (chemically pure grade) was purified by numerous recrystallizations and had m. p. 238°. Salicylic acid (chemically pure grade) was also purified by numerous recrystallizations and had m. p. 159.8°. Succinic acid (chemically pure grade) was recrystallized and then had m. p. 184.5°. Adipic acid (chemically pure) had m. p. 151°.

The visual-polythermal method was employed for investigation of the fusion behavior and for determination of the melting points of the pure substances. We established the temperatures of appearance of the first crystals by cooling down of the fused mixture, and we determined the temperatures of disappearance of the last crystals on melting. The agreement between the two temperatures indicated that equilibrium had been attained from both directions [4].

The substance was placed in a test tube provided with a thermometer and stirrer. More uniform heating and cooling was effected by putting the test tube in a glass housing.

Densities were measured with the Reno pycnometer with a narrow neck and a capacity of 4.5 ml. Viscosities were determined in an Ostwald viscometer of the open type.

Electrical conductivity was measured by the Kohlrausch method in a closed cell using a smooth platinum electrode. The current source was a lamp generator of sonic frequency with an amplifier. For the purpose of improving the accuracy of measurement, the minimum of the current was stepped up with a two-lamp amplifier and then picked up on the recorder (high-ohmic telephones and "magic eye").

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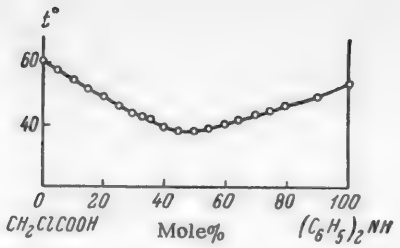

Fig. 1. Fusibility curve of the system diphenylamine–monochloroacetic acid.

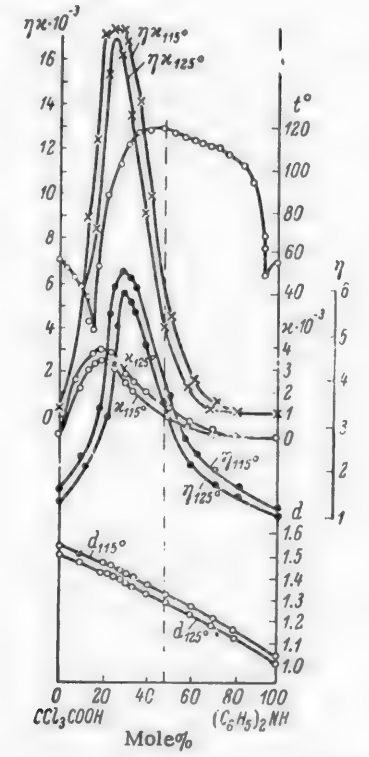

Fig. 2. Curve of fusion, viscosity (η), density (d), specific electrical conductivity (κ) and corrected electrical conductivity ($\kappa \cdot \eta$) of the system diphenylamine–trichloroacetic acid.

Densities, viscosities and electrical conductivities were measured in a glycerol thermostat which enabled the temperature to be kept constant to within 0.1°.

Mixtures were made up by individual weighings. Concentrations were calculated in molar percentages; viscosities were expressed in centipoises.

Examination of binary systems of diphenylamine with organic acids. The system diphenylamine–monochloroacetic acid had not previously been studied. We investigated it by the fusion method (Fig. 1). The fusion curve consists of two branches – diphenylamine and monochloroacetic acid – which intersect at the eutectic point corresponding to 50 mole% and 37.5°.

System diphenylamine–trichloroacetic acid. This was here examined for the first time, using data for fusion, viscosity, density and specific electrical conductivity (Fig. 2). The fusion curve has a maximum corresponding to 50 mole% of diphenylamine, indicating the formation in the solid phase of a compound of equimolar composition which melted considerably higher than the pure components. Whereas the melting point of the highest melting component (trichloroacetic acid) is 59°, the compound melts at 112.5°. The fusion curve has two eutectics – at 50.5° and 97 mole%, and at 25° and 15 mole% of diphenylamine. The specific electrical conductivity, viscosity and density of the system were examined at 115 and 125°. The viscosity isotherms contain a maximum corresponding to 30 mole% of diphenylamine in the mixture. The density isotherms are slightly concave to the axis of concentrations.

The specific electrical conductivity isotherms contain a maximum corresponding to 25 mole% of diphenylamine in the mixture; the maximum is considerably higher than that of the component with the highest conductivity. Correction of the electrical conductivity for viscosity $\kappa \cdot \eta$ does not eliminate the maximum but merely shifts it slightly in the direction of diphenylamine. In the opinion of some investigators [4] the chemical compound in the system is characterized by a minimum of electrical conductivity. A whole series of systems of this type was investigated, however, and in these the reaction is reflected by a maximum of electrical conductivity that does not disappear when the viscosity correction is applied [5-7]. According to M. I. Usanovich [8], the persistence of the maximum on the curve of corrected electrical conductivity testifies to the occurrence of acid–base interaction in the system. In the present case, however, the position of the maximum is no guide as to the composition of the compound formed in the liquid phase.

System diphenylamine–p-nitrobenzoic acid. We studied this system on the basis of fusion data (Fig. 3). The two branches of the curve intersect at a eutectic corresponding to a 98 mole% of diphenylamine.

System diphenylamine–salicylic acid. We also studied this system only by fusion observations (Fig. 4). The fusion curve comprises a long branch of diphenylamine. The eutectic point is considerably shifted onto the side of diphenylamine and corresponds to 97 mole% of the latter.

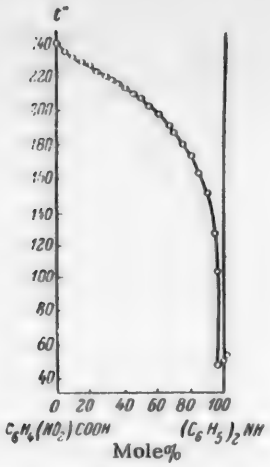

Fig. 3. Fusion curve of the system diphenylamine–p-nitrobenzoic acid.

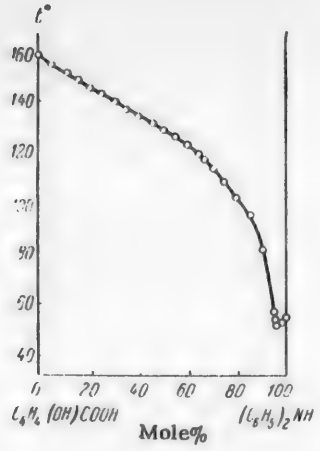

Fig. 4. Fusion curve of the system diphenylamine–salicylic acid.

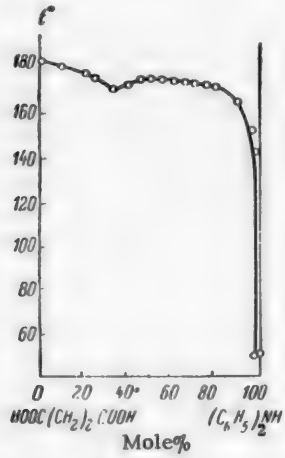

Fig. 5. Fusion curve of the system diphenylamine–succinic acid.

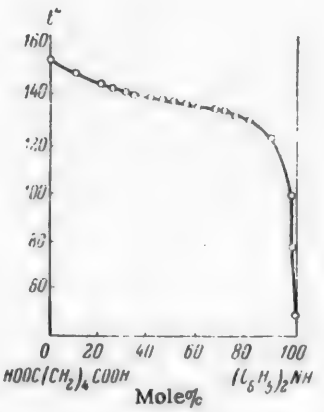

Fig. 6. Fusion curve of the system diphenylamine–adipic acid.

System diphenylamine–succinic acid. The fusion curve (Fig. 5) contains a maximum corresponding to the compound $C_{12}H_{11}N \cdot C_4H_6O_4$ with m. p. 177.5°, and two eutectic points – at 172° and 33.4 mole%, and 52° and 99.5 mole% of diphenylamine.

System diphenylamine–adipic acid. A slight fall in melting point is observed on the portion of the fusion diagram (Fig. 6) from 0 to 90 mole%, which indicates closeness to the limiting mutual solubility of the components. Fusion curves of similar form were obtained by F. V. Alekseev [9] when studying the system salicylic acid–water and by O. A. Osipov [10] for the system butyric acid–picric acid.

DISCUSSION OF RESULTS

It follows from the results obtained that systems formed by organic acids with diphenylamine do not exhibit chemical interaction in the overwhelming majority of cases.

In a study of the interaction of diphenylamine with acetic acid, N. A. Trifonov [11] established the absence of formation of any chemical compound between the components. Introduction of the electronegative chlorine atom into the acetic acid molecule facilitates cleavage of a hydrogen ion, i. e., it intensifies the acidity of the compound. Hence in substances of basic character we should expect intensification of interaction in the order:

$$CH_3COOH \rightarrow CH_2ClCOOH \rightarrow CHCl_2COOH \rightarrow CCl_3COOH.$$

Our investigations showed that the introduction of one chlorine atom into the acetic acid molecule does not alter the behavior, and diphenylamine does not react with monochloroacetic acid. Study of the interaction of diphenylamine with trichloroacetic acid revealed the existence of the compound $C_{12}H_{11}N \cdot CCl_3COOH$ in the solid phase; it occupies a large portion of the phase diagram of the system. The viscosity curves possess a maximum, which points to interaction of the components also in the liquid phase. This is confirmed by the form of the curves of specific and corrected electrical conductivity which also exhibit maxima. The position of the maxima on the above-mentioned curves does not correspond to the composition of a compound. The density curves are convex, indicating contraction in the system.

Lengthening of the chain of the acid molecule usually leads to weakening of the acidic properties of a compound. Propionic and butyric acids accordingly do not react with diphenylamine [12]. On the other hand, lauric acid [2], with a very much smaller dissociation constant than that of butyric acid (10^{-12} and $1.48 \cdot 10^{-5}$, respectively) reacts with diphenylamine to form an equimolar compound.

Reaction of benzoic acid with diphenylamine was studied by A. Baskov [13] who made observations on fusion, viscosity and electrical conductivity. None of his data reflected interaction between the components. Introduction of electronegative substituents into benzoic acid intensifies the mobility of the hydrogen of the carboxyl group, especially if the substituent is in the ortho-position. Thus, salfcylic acid gives molecular compounds with amines with which benzoic acid does not interact, for example, with α- and β-naphthylamines [14]. However, as our researches showed, diphenylamine does not react with salicylic acid. Nor does the introduction of a nitro group into the molecule of benzoic acid alter the behavior. Diphenylamine does not form compounds with p-nitrobenzoic acid.

In the system diphenylamine—succinic acid the fusion method revealed the formation of an equimolar compound. Diphenylamine does not react with adipic acid; a tendency to form layers is observed in this system, as reflected by the form of the fusion curve.

Consequently, the introduction of another benzene ring into the aniline molecule has a remarkably strong depressant effect on its activity; diphenylamine is less reactive than aniline.

SUMMARY

1. Systems formed by diphenylamine with monochloroacetic, salicylic, p-nitrobenzoic, succinic and adipic acids were studied by the fusion method.

2. The phase diagrams of all of these systems, except with succinic acid, indicate absence of chemical interaction between the components.

3. The system formed by diphenylamine with trichloroacetic was studied by observations on fusion, density, viscosity and electrical conductivity.

4. It was established that the presence of two benzene rings in the diphenylamine molecule greatly lowers its susceptibility to complex formation.

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PHYSICOCHEMICAL ANALYSIS OF THE SYSTEM ETHYLENEDIAMINE – ALLYL MUSTARD OIL

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Systems formed by mustard oils with secondary amines are typical rational systems [1]. In an investigation of the viscosity of systems of this class, N. S. Kurnakov and S. F. Zhemchuzhnyi showed [2] that they undergo reaction according to the equation

$$S{=}C{=}NR + NHR_2^1 = CS(NHR)(NR_2^1),$$

with formation of substituted thioureas; the latter are transparent substances that do not break down under normal conditions. Curves of all of the physical properties of such systems possess a singular point whose position corresponds to the composition of the compound.

At the present time systems that have been closely examined are those comprising on the one hand allyl mustard oil and on the other hand aniline, piperdine, the isomeric toluidines; also systems of phenyl mustard oil with diethylamine, methyl- and ethylaniline, etc. [1-4].

In the present work we studied the interaction in the system allyl mustard oil–ethylenediamine by methods of physicochemical analysis.

For this purpose we made use of measurements of viscosity, density, refractive index, and boiling point; we also determined the composition of the vapor.

The components of the system were carefully purified. Allyl mustard oil was dried with freshly calcined calcium chloride and redistilled. We selected the cut boiling at 149.5-150.5° (752.7 mm). We isolated ethylenediamine from its hydrochloride, and dried it first with solid potassium hydroxide and then with metallic sodium before distilling it over the latter to obtain a product with b. p. 116.5-116.7° at 753.5 mm; $n^{20}D$ and $n^{18}D$ 1.5273 and 1.4578, respectively.

Considerable heat was released when the components were mixed, and caused the liquid to boil. In order to avoid losses, the substances were gradually mixed in Landolt vessels while being adequately cooled.

The viscosity was measured at 40° in two Ostwald viscometers of the closed type with capillaries of different diameters.

The viscometer with the larger diameter of capillary was used for the more viscous mixtures (50-80 mole% of mustard oil). This viscometer was calibrated with castor oil. Densities were measured in a pycnometer with a capacity of 1.2173 ml. The refractive index was determined at 35° in an Abbe refractometer. Results of measurements of these physical properties are presented in Table 1.

Boiling points and vapor compositions were determined in an apparatus of our own design operating on the principle of the ebullioscopic apparatus of V. A. Kireev [5]. The pressure in the apparatus was maintained to an accuracy of ±0.3 mm Hg by a manostat with electromagnetic control. Boiling points of the system were determined at 100 and 200 mm Hg; vapor compositions were determined at 100 mm. Results are in Table 2.

The viscosity isotherm of the system (Fig. 1) consists of two branches, convex in relation to the axis of composition and intersecting in a sharp singular point at 66.7 mole% of mustard oil, thereby reflecting the presence

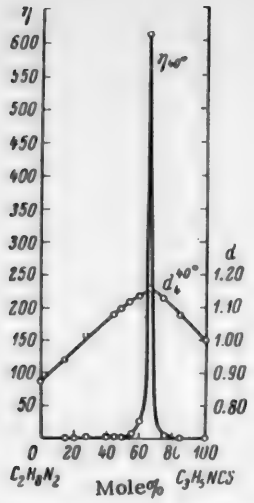

Fig. 1. Viscosity and density of the system ethylenediamine–allyl mustard oil.

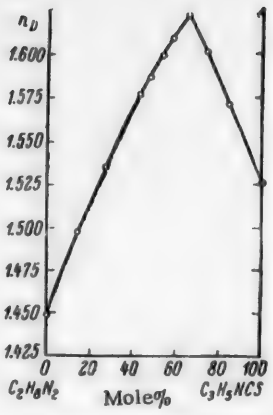

Fig. 2. Isotherm of the refraction index in the system ethylenediamine–allyl mustard oil.

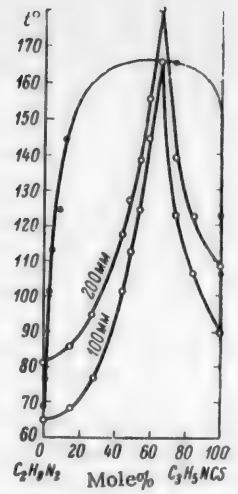

Fig. 3. Boiling points and vapor composition in the system ethylenediamine–allyl mustard oil.

TABLE 1

C_3H_5NCS in sol'n (mole%)	η^{40} (in poises)	d_4^{40}	n_D^{35}
0.00	0.007611	0.8713	1.4496
15.00	0.02956	0.9385	1.4974
27.94	0.06678	1.0120	1.5350
45.15	0.71457	1.0803	1.5775
49.48	1.55380	1.0963	1.5863
54.96	6.48500	1.1156	1.5994
59.94	24.7040	1.1333	1.6083
66.70	610.970	1.1548	1.6217
75.02	2.81410	1.1263	1.6010
85.10	0.55480	1.0740	1.5712
100.0	0.00592	0.9985	1.5252

TABLE 2

C_3H_5NCS (mole%)		Boiling point (pressures in mm Hg)	
in liquid phase	in vapor at 100 mm	100	200
0.00	0.0	65.0	81.3
15.00	0.2	68.6	85.8
27.94	1.1	76.7	94.8
45.15	3.1	101.5	117.6
49.48	4.6	113.1	127.3
54.96	9.8	124.5	138.7
59.94	13.6	144.7	155.7
66.70	74.7	165.6	179.5
75.02	100.0	123.1	139.0
85.10	100.0	106.7	122.5
100.0	100.0	89.8	108.5

in the system of the undissociated compound $C_2H_8N_2 \cdot 2C_3H_5NCS$. A striking feature is the enormous value of the viscosity of this substituted thiourea (η^{40} = 610.97 poises) or 80,275 times higher than the viscosity of ethylenediamine (the most viscous component). The prepared ethylenedi(allylthiourea) is considerably more viscous than the product of interaction in the system phenyl mustard oil–diethylamine [2], hitherto considered to be the most viscous of the substituted thioureas.

The high value of the viscosity of such compounds is usually associated not only with their strong supercooling but also with considerable association [4].

The isotherm of the density d^{40}_4 of the system comprises two nearly rectilinear branches (Fig. 1) intersecting at an acute angle to give a singular point corresponding to 66.7 mole% of oil and characterizing the formation of the above-noted substituted thiourea.

The isotherm of the refraction index $n^{35}D$ (Fig. 2) has a well-defined singular maximum corresponding to 66.7 mole% of oil, which agrees with the viscosity and density data in indicating the formation of an undissociated compound in the system.

Chemical interaction in the system is reflected in the results of the ebulliometric examination of the system. The boiling point curves (Fig. 3) for 100 and 200 mm Hg, plotted from the data of Table 2, each consist of two branches that intersect in a singular point whose position does not alter with changing pressure; it corresponds to the compound $C_2H_8N_2 \cdot 2C_3H_5NCS$. The condensation curve, obtained for 100 mm Hg, has a

maximum that touches the liquid line at its singular point (Fig. 3). The singular point is weakly developed on the condensation curve although there is no doubt as to its existence.

A noteworthy feature is the form of the condensation curve. Its branches pass close to the ordinates of the components and then sharply inflect to come together at an acute angle. This may be due to the resulting compound having a high boiling point and a higher value for the heat of vaporization. Due to this, the vapor phase of the majority of the solutions, apart from those is close proximity to the compound, consists of nearly pure components.

In the light of the results obtained, the system ethylenediamine–allyl mustard oil must be regarded as a rational system. Inspection of the property curves shows that their singular points, including the point on the boiling isobar, correspond to the same composition – 66.7 mole% of allyl mustard oil. The azeotropic mixture in this system is probably, as in all rational systems, a true chemical compound. We have in this system a striking example of a singular boiling isobar whose course is consistent with the isotherms of viscosity and certain other properties.

SUMMARY

1. The system ethylenediamine–allyl mustard oil was investigated with the help of data for viscosity, density, refractive index and boiling point (at 100 and 200 mm Hg). The vapor composition over the solutions was also determined.

2. Only one compound is formed in the system – ethylene-di(allylthiourea), $C_2H_8N_2 \cdot 2C_3H_5CNS$. It is undissociated under normal conditions.

The system is an example of a rational system.

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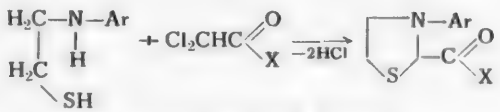
ETHYLENE SULFIDE IN THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS WITH TWO HETERO-ATOMS

VII. 3-ARYLTHIAZOLIDINE-2-CARBOXYLIC ACIDS AND THEIR DERIVATIVES

Iu. K. Iur'ev and S. V. Diatlovitskaia

The chemistry of thiazolidine and its derivatives has been studied most thoroughly and minutely in the case of thiazolidine-4-carboxylic acid, this being an important structural component of the penicillin molecule. As regards thiazolidine-2-carboxylic acid, neither the substance itself nor its derivatives has been reported up to now.

In one of our earlier works [1] we showed that N-(β-mercaptoethyl) arylamines readily enter into condensation with 1,1-dihaloalkanes, forming 3-arylthiazolidines. In the present work we carried out the same type of condensation with dichloroacetic acid, its amide, and its ester and obtained 3-arylthiazolidine-2-carboxylic acids, their amides, and their esters, respectively; from the latter we prepared the hydrazides.



(X = OH, NH_2, OC_2H_5, $NHNH_2$)

As also in the case of condensation of N-(β-mercaptoethyl) arylamines with methylene bromide [1], linear condensation products were obtained, together with 3-arylthiazolidine-2-carboxylic acids and their derivatives, in the condensations described in the present work. On distillation in vacuo they boiled over a wide range with appreciable decomposition and were not further investigated.

Study of the properties of 3-arylthiazolidine-2-carboxylic acids revealed that they decompose easily on treatment with acids. In connection with this, we could not prepare 3-o-tolyl- or 3-o-anisylthiazolidine-2-carboxylic acid either by the method given above or by hydrolysis of the esters of these acids with either 2 N hydrochloric or 50% acetic acid; when these esters were boiled with barium hydroxide solution, cleavage of the thiazolidine ring also occurred (appearance of a positive reaction for the sulfhydryl group).

The esters of 3-p-tolyl- and 3-p-anisylthiazolidine-2-carboxylic acids occur as colorless crystals. The esters of 3-phenyl-, 3-o-tolyl-, and 3-o-anisylthiazolidine-2-carboxylic acids are viscous oils which partially decompose on distillation in vacuo, owing to which it was impossible to obtain them in a perfectly pure state. Therefore, in order to characterize these esters, we prepared from them the corresponding 3-arylthiazolidine-2-carboxylic acid hydrazides.

Introduction of negatively charged groups ($-NH_2$, $-NH-NH_2$) into the carboxyl group led to the production of 3-arylthiazolidine-2-carboxylic acid derivatives which were somewhat more stable than the acids themselves; the amides and hydrazides of these acids do not decompose on strong heating, and they melt without decomposition (with the exception only of 3-phenyl- and 3-p-tolylthiazolidine-2-carboxylic acid amides); they are also quite stable to the action of acidic agents and decompose only on boiling with concentrated hydrochloric acid for 30-40 min.

EXPERIMENTAL

3-Arylthiazolidine-2-carboxylic Acids

3-Phenylthiazolidine-2-carboxylic acid. A mixture of 7.65 g (0.05 mole) of dichloroacetic acid, 7.5 g (0.09 mole) of anhydrous sodium acetate, 10.6 g (0.1 mole) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 4 hrs in a water bath. The solid residue, obtained after driving off the alcohol, was put into a separatory funnel and shaken with a mixture of 1 N hydrochloric acid (100 ml) and ether (40 ml) until the residue was fully dissolved. After the ether layer was drawn off, the aqueous solution was extracted several more times with ether (a test sample of the aqueous solution had to remain clear on acidification with 2 N hydrochloric acid). The ether extract was dried with anhydrous magnesium sulfate.

After the ether was driven off, the residue crystallized. The crystals of 3-phenylthiazolidine-2-carboxylic acid were filtered out from the oil, washed with cold alcohol, and recrystallized from alcohol; m. p. 169-170° (decomp.). Yield, 5.2 g (50%).

Found %: C 57.13, 56.93; H 5.31, 5.40; N 6.55, 6.46; S 15.19, 15.38. M 209.0, 210.0. $C_{10}H_{11}O_2NS$. Calculated %: C 57.39; H 5.30; N 6.69; S 15.32; M 209.3.

3-p-Tolylthiazolidine-2-carboxylic acid. From 8.35 g of N-(β-mercaptoethyl)-p-toluidine and 7.75 g of dichloroacetic acid, 4.8 g (43%) of 3-p-tolylthiazolidine-2-carboxylic acid was obtained by the method given above; m. p. 164.5-165° (decomp.) (from alcohol).

Found %: C 59.59, 59.41; H 6.12, 6.22; N 6.11, 6.08. M 222.3, 223.2. $C_{11}H_{13}O_2NS$. Calculated %: C 59.16; H 5.87; N 6.27. M 223.3.

3-p-Anisylthiazolidine-2-carboxylic acid. A mixture of 9.15 g (0.05 mole) of N-(β-mercaptoethyl)-p-anisidine, 12.9 g (0.1 mole) of dichloroacetic acid, 7.5 g (0.09 mole) of anhydrous sodium acetate, 10.6 g (0.1 mole) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 5 hrs in a water bath. To the oil, obtained after driving off the ether, was added 20 ml of 2 N hydrochloric acid, and the mixture was extracted with ether. (Part of the oily residue failed to dissolve in the ether and adhered to the walls of the flask and the separatory funnel in the form of tar.) The ether extract was dried with anhydrous magnesium sulfate.

The residue, obtained after driving off the ether, crystallized. The crystals of 3-p-anisylthiazolidine-2-carboxylic acid were filtered out from the oil, washed with cold alcohol, and recrystallized from alcohol; m. p. 130-130.5° (decomp.). Yield, 2.6 g (22%).

Found %: C 55.47, 55.50; H 5.60, 5.67; N 5.81. M 238.8, 240.0. $C_{11}H_{13}O_3NS$. Calculated %: C 55.21; H 5.48; N 5.85. M 239.3.

3-Arylthiazolidine-2-carboxylic acids are readily soluble in ether, acetone, and dichloroethane, poorly soluble in alcohol and benzene, and insoluble in water.

On heating with concentrated hydrochloric acid for 5-10 min 3-arylthiazolidine-2-carboxylic acids are cleaved; a positive reaction for the sulfhydryl group appears; on boiling with a concentrated solution of alkali the positive reaction for the sulfhydryl group appears after 1.5-2 hrs.

3-Arylthiazolidine-2-carboxylic Acid Amides

Procedure. A mixture of 0.05 mole of the N-(β-mercaptoethyl)arylamine, 0.075 mole (9.6 g) of dichloroacetamide, 0.06 mole (5 g) of anhydrous sodium acetate, 0.066 mole (7.5 g) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 4 hrs in a water bath. After distilling off the alcohol the solid residue was treated 5 times by shaking with a mixture of ether and water in a separatory funnel. The undissolved solid part – the 3-arylthiazolidine-2-carboxylic acid amide – was filtered out, washed with ether, and recrystallized from alcohol. The ethereal extract was dried with anhydrous magnesium sulfate. An additional small amount of amide crystals separated out from the oil obtained after driving off the ether.

TABLE 1

Amides	Yield in %	Melting point	C (%) found	C (%) calc.	H (%) found	H (%) calc.	N (%) found	N (%) calc.
3-Phenylthiazolidine-2-carboxylic acid amide	30	171—172° (decomp.)	57.69, 57.43	57.66	5.96, 5.92	5.81	13.25, 13.21	13.45
3-p-Tolylthiazolidine-2-carboxylic acid amide	38	192.5—193 (decomp.)	59.64, 59.60	59.43	6.32, 6.38	6.35	12.40, 12.61	12.60
3-o-Tolylthiazolidine-2-carboxylic acid amide	21.5	155—155.5	59.06, 59.01	59.43	6.38, 6.58	6.35	12.30, 12.31	12.60
3-p-Anisylthiazolidine-2-carboxylic acid amide	27	162—163	55.84, 55.74	55.44	6.15, 5.96	5.92	12.08, 11.86	11.76
3-o-Anisylthiazolidine-2-carboxylic acid amide	25	149—150	55.25, 55.16	55.44	6.20, 6.19	5.92	11.85, 11.98	11.76

The 3-arylthiazolidine-2-carboxylic acid amides prepared in the present work are listed in Table 1.

3-Arylthiazolidine-2-carboxylic acid amides are soluble in acetone and dichloroethane, poorly soluble in alcohol, ether, and benzene, and insoluble in water.

Esters and Hydrazides of 3-Arylthiazolidine-2-carboxylic Acids

Ethyl-3-phenylthiazolidine-2-carboxylate. A mixture of 7.65 g (0.05 mole) of N-(β-mercaptoethyl)aniline, 11.8 g (0.075 mole) of ethyl dichloroacetate, 5 g (0.06 mole) of anhydrous sodium acetate, 7.5 g (0.066 mole) of anhydrous sodium carbonate, and 50 ml of anhydrous alcohol was boiled for 5 hrs in a water bath.

After the alcohol was driven off, the solid residue, permeated with oil, was shaken in a separatory funnel with a mixture of water and ether until it was complete dissolved; the ether layer was drawn off, and the aqueous solution was then extracted with ether three more times. The combined extracts were dried with anhydrous magnesium sulfate.

After the ether was driven off, the dark-red oil was extracted for 12 hrs in an extractor with light petroleum ether (b. p. 30-50°). After the petroleum ether was driven off, there was obtained 6.05 g (51%) of a yellowish oil, which after distillation in vacuo in a current of nitrogen had the following constants:

B. p. 163-164° (2 mm), $n^{20}D$ 1.5795, d^{20}_4 1.1846, MR_D 66.62. $C_{12}H_{15}O_2NS\,F_3$. Calculated 65.38. Found %: C 61.08, 61.02; H 6.62, 6.69; N 5.65, 5.74. $C_{12}H_{15}O_2NS$. Caculated %: C 60.73; H 6.37; N 5.90.

Ethyl 3-p-tolylthiazolidine-2-carboxylate. Into reaction were brought 8.35 g of N-(β-mercaptoethyl)-p-toluidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other components of the mixture.

After the corresponding treatment of the reaction product an oil was obtained which partly crystallized on standing. The crystals – ethyl 3-p-tolylthiazolidine-2-carboxylate – were filtered out and were dissolved on heating in light petroleum ether (b. p. 30-50°); the filtrate was extracted with the latter in an extractor. The extracts obtained were combined, and after the solvent was driven off, a crystalline residue separated out; m. p. 57-57.5° (from alcohol). Yield, 5.2 g (41.5%).

Found %: C 62.08, 62.26; H 6.93, 6.80; N 5.61, 5.50. $C_{13}H_{17}O_2NS$. Calculated %: C 62.12; H 6.82; N 5.57.

Ethyl 3-o-tolylthiazolidine-2-carboxylate. Into reaction were brought 8.35 g of N-(β-mercaptoethyl)-o-toluidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other components of the mixture.

After the corresponding treatment of the reaction product, the following fractions were isolated on distillation in vacuo of the resulting oil in a current of nitrogen: 1st fraction, b. p. up to 125° (3 mm), 0.3 g; 2nd fraction, b. p. 160-167° (3 mm), 6.1 g (49%); residue – tar.

Fraction 1 was unchanged ethyl dichloroacetate. Fraction 2 – ethyl 3-o-tolylthiazolidine-2-carboxylate – was redistilled:

B. p. 164-165° (3 mm), $n^{20}D$ 1.5630, d^{25}_4 1.1515, MR_D 70.90. $C_{13}H_{17}O_2NSF_3$. Calculated 70.00. Found %: C 62.78, 62.77; H 6.72, 6.88; N 5.35, 5.28. $C_{13}H_{17}O_2NS$. Calculated %: C 62.12; H 6.82; N 5.57.

Ethyl 3-p-anisylthiazolidine-2-carboxylate. When the oily product of the reaction of 9.15 g of N-(β-mercaptoethyl)-p-anisidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other reaction components was distilled in vacuo in a current of nitrogen at 176-180° (2 mm), a yellow oil was isolated, which partly crystallized on standing. The crystals – ethyl 3-p-anisylthiazolidine-2-carboxylate – were pressed out and recrystallized from alcohol; m. p. 48-48.5°. Yield, 4.01 g (30%).

Found %: C 58.56, 58.67; H 6.47, 6.65; N 5.13, 5.29. $C_{13}H_{17}O_3NS$. Calculated %: C 58.40; H 6.41; N 5.24.

Ethyl 3-o-anisylthiazolidine-2-carboxylate. When the product of the reaction of 9.15 g of N-(β-mercaptoethyl)-o-anisidine, 11.8 g of ethyl dichloroacetate, and the above-stated quantities of the other reaction components was distilled in vacuo in a current of nitrogen, there was isolated 4.3 g (32.5%) of ethyl 3-o-anisylthiazolidine-2-carboxylate (yellow oil):

B. p. 180-181° (3 mm), $n^{20}D$ 1.5730, d^{20}_4 1.1885, MR_D 74.12. $C_{13}H_{17}O_3NSF_3$. Calculated 71.64. Found %: C 59.27; H 6.70; N 5.42, 5.42. $C_{13}H_{17}O_3NS$. Calculated %: C 58.40; H 6.41; N 5.24.

3-Arylthiazolidine-2-carboxylic Acid Hydrazides

Procedure. A mixture of the ethyl 3-arylthiazolidine-2-carboxylate, hydrazine hydrate, and alcohol (taken in the ratio, 1 g of the ester to 1 ml of hydrazine hydrate and 1 ml of alcohol) was boiled for 10 min, until a clear solution was obtained. The 3-arylthiazolidine-2-carboxylic acid hydrazide crystals, which separated out

TABLE 2

Hydrazides	Yield in %	Melting point	C (%)		H (%)		N (%)	
			found	calc.	found	calc.	found	calc.
3-Phenylthiazolidine-2-carboxylic acid hydrazide	76	135.5—136°	53.50, 53.58	53.79	5.92, 5.98	5.87	18.72, 18.60	18.82
3-p-Tolylthiazolidine-2-carboxylic acid hydrazide	100	176—176.5	55.65, 55.88	55.67	6.39, 6.38	6.37	17.54, 17.50	17.71
3-o-Tolylthiazolidine-2-carboxylic acid hydrazide	74	130.5—131	55.91, 55.77	55.67	6.21, 6.15	6.37	17.80, 17.85	17.71
3-p-Anisylthiazolidine-2-carboxylic acid hydrazide	100	143.5—144	51.90, 51.93	52.15	6.06, 6.02	5.97	16.16, 16.32	16.59
3-o-Anisylthiazolidine-2-carboxylic acid hydrazide	70	103—104	52.26, 52.07	52.15	6.08, 5.79	5.97	16.55, 16.54	16.59

on cooling, were filtered off; several milliliters of water was added to the filtrate, and the crystals, which precipitated were again filtered off. The crystals were washed with ether, dried, and recrystallized from water.

The 3-arylthiazolidine-2-carboxylic acid hydrazides, prepared in the present work, are listed in Table 2.

3-Arylthiazolidine-2-carboxylic acid hydrazides are soluble in alcohol, benzene, acetone, and dichloroethane; they are insoluble in ether and water.

SUMMARY

1. The reaction of N-(β-mercaptoethyl)arylamines with dichloroacetic acid leads to 3-arylthiazolidine-2-carboxylic acids, which are not described in the literature. In the present work 3-phenyl-, 3-p-tolyl-, and 3-p-anisylthiazolidine-2-carboxylic acids were prepared in this way.

2. The condensation of N-(β-mercaptoethyl)arylamines with dichloroacetamide, which takes a similar course, leads to 3-arylthiazolidine-2-carboxylic acid amides, which are not described in the literature. In the present work 3-phenyl-, 3-p-tolyl-, 3-o-tolyl-, 3-p-anisyl-, and 3-o-anisylthiazolidine-2-carboxylic acid amides were prepared in this way.

3. The condensation of N-(β-mercaptoethyl)arylamines with ethyl dichloroacetate leads to the ethyl esters of 3-phenyl-, 3-p-tolyl-, 3-o-anisylthiazolidine-2-carboxylic acids, which are not described in the literature; the esters are converted to the corresponding hydrazides on treatment with hydrazine hydrate.

LITERATURE CITED

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* Original Russian pagination. See C. B. translation.

REACTION OF 1,3-DICHLOROBUTENE-2 WITH ISOPRENE AND DIVINYL UNDER THE INFLUENCE OF $FeCl_3$. III

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The results of a study of the reaction of 1,3-dichlorobutene-2 with chloroprene under the influence of Friedel-Crafts-Gustavson catalysts were given in the preceding report.* Continuing the work in the same direction, we studied the reaction of 1,3-dichlorobutene-2 with isoprene and divinyl in the presence of $FeCl_3$. In both cases the formation of products of low molecular weight, as well as resinous products, was observed.

We attempted to use $AlCl_3$, also, as catalyst; however, it was impossible to isolate the primary product in this case. Subsequent experiments, therefore, were conducted only with $FeCl_3$ catalyst at a concentration not exceeding 0.25 mole%, since at greater concentrations the amount of products of high molecular weight increased with simultaneous decrease of the yield of the primary addition product, which hindered the isolation of the latter.

Both in reactions with isoprene and in reaction with divinyl, the composition of the products is strongly affected by the ratio of the initial substances, the yield of the primary addition product increasing with increase in the excess of 1,3-dichlorobutene-2.

As a consequence of the addition of 1,3-dichlorobutene-2 to isoprene, the formation of 6 reaction products, depending on the course of the addition: 1,4; 4,1; 1,2; 2,1; 3,4; or 4,3; may be expected as the primary result. It was found that addition takes place mainly in the 1,4-position with formation of compound (I).

$$CH_3CCl{=}CHCH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CHCH_2Cl. \qquad \text{(I)}$$

$$CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{-}CH{=}CH_2 \qquad \text{(II)}$$

The structure of the product formed was proved by ozonization. Among the decomposition products of the ozonide were found acetic (72.63%), chloroacetic (82.17%), and levulinic (85.7%) acids and tars.

It follows from the ozonolysis data that 1,3-dichlorobutene-2 adds to isoprene mainly in the 1,4-position (Formula I), which is also in accord with the distribution of electron density in the isoprene molecule (II).

On the basis of such an electron density distribution in the isoprene molecule it could be assumed that the addition of the complex $CH_3CCl{=}CHCH_2^+ \cdot FeCl_4^-$ to isoprene would take place mainly in the 1,4-position with formation of compound (I); other courses are less probable.

Products of the addition of two molecules of 1,3-dichlorobutene-2 to one of isoprene were not found in the reaction mixture.

The polymers were divided into narrow fractions by precipitating them with methyl alcohol from benzene solution. The isolated fractions were characterized by their molecular weight, and also by analysis for total chlorine and saponifiable chlorine. Their structures were not determined, owing to their complexity.

* J. Gen. Chem. 28, 574 (1958). [Original Russian pagination. See C.B. Translation.

The presence of saponifiable chlorine, established by analyses of individual fractions, gives grounds for assuming that the polymer is formed by stepwise condensation from one 1,3-dichlorobutene-2 molecule and n molecules of isoprene. Here telomerization also takes place, as in the case of the reaction of 1,3-dichlorobutene-2 with chloroprene.

As a consequency of the addition of 1,3-dichlorobutene-2 to divinyl the formation of three different reaction products, depending on the course of the addition (1,4, 1,2, or 2,1), may be expected as the primary result. The method of ozonolysis was used to establish the structure. Among the decomposition products of the ozonide were found acetic (72.4%), chloroacetic (71.8%), and succinic (75.2%) acids. The ozonolysis data show that the addition of 1,3-dichlorobutene-2 to divinyl, also, occurs mainly in the 1,4-position with formation of the compound $CH_3CCl=CHCH_2CH_2CH=CHCH_2Cl$.

As in the case of isoprene, products of the addition of two molecules of 1,3-dichlorobutene-2 to one of divinyl were not found in the reaction mixture.

The results of the investigation confirmed that, as in the cases of chloroprene and isoprene, telomerization also occurs here with formation of compounds of higher molecular weight.

EXPERIMENTAL

1. Reaction of 1,3-Dichlorobutene-2 with Isoprene

In the presence of 0.487 g of $FeCl_3$ (0.25 mole%), 122.2 g of 1,3-dichlorobutene-2 and 16.4 g of isoprene were kept at 20° in a round-bottomed flask with a reflux condenser in a nitrogen atmosphere for 6 hrs. In the course of the work it turned out that, owing to the exothermic character of the polycondensation reaction, the temperature rose and resinification occurred. The reaction product was washed with dilute hydrochloric acid and then water, and dried with Na_2SO_4, after which the unreacted starting materials were driven off. The residue was distilled in vacuo. One fraction, b. p. 65-75° at 3 mm (4.69 g), and a residue (polymer, 8.2 g) were obtained thereby. By redistillation of this fraction, 3.07 g of product was obtained.

B. p. 70-72° at 3 mm, d^{20}_4 1.0578, $n^{20}D$ 1.4887, MR_D 52.72; calculated 52.56. Found %: Cl 36.36, sapon. Cl 18.17. M 187; bromine number 167.7. $C_9H_{14}Cl_2$. Calculated %: Cl 36.79, sapon. Cl 18.39. M 193; bromine number 165.8.

Corresponding fractions from several experiments were combined and ozonized. For ozonization 7.72 g of the product was taken. After decomposition of the ozonide with water and a 3% H_2O_2 solution the acid mixture did not contain formic acid (test with $AgNO_3$ solution). The aqueous solution of acids was filtered to remove tars (0.921 g). After distillation of the volatile acids in vacuo (at 35-40°), a tarry, crystalline product (4.78 g) remained in the flask.

Hydrochloric acid was determined from the chlorine content in the volatile-acid mixture.

Found 1.228 g (84.17%) HCl.

The acetic acid was isolated as the silver salt by treatment of the distilled volatile-acid solution with silver oxide; after recrystallization the salt was analyzed.

Found %: Ag 63.98. $C_2H_3O_2Ag$. Calculated %: Ag 64.59.

The quantity of acetic acid was calculated from the total acidity of the volatile-acid mixture, since no other acids were found in the form of the silver salts. For neutralization of the volatile acids 3.51 g of KOH was required; 1.883 g of this was used to neutralize hydrochloric acid; hence 1.627 g of KOH was used for neutralization of acetic acid, which corresponds to 1.743 g (72.63%) of acetic acid.

The chloroacetic acid, isolated from the crystalline distillation residue, had b. p. 67-69° at 4 mm and m. p. 58-59° (according to literature data, m. p. 61.5°).

Found %: Cl 36.35. Equiv.: 603.14. $C_2H_3O_2Cl$. Calculated %: Cl 37.57. Equiv.: 592.6.

The quantity of chloroacetic acid (82.17%) was calculated from the chlorine content in the crystalline product (1.36 g, which corresponds to 3.62 g of chloroacetic acid).

The levulinic acid, which was also isolated from the crystalline residue, distilled with decomposition (b. p. 80-85° at 4 mm); its crystals melted at 34-35° (according to literature data, m. p. 33.5°).

Found: equiv. 465.37. $C_5H_8O_3$. Calculated: equiv. 482.30.

The quantity of levulinic acid was calculated from the total acidity of the aqueous solution. For neutralization of the latter, 5.655 g of KOH was required; of this the neutralization of hydrochloric acid used 1.863 g, that of acetic acid used 1.627 g, and that of chloroacetic acid used 2.145 g. Since no other acids were found, the rest of the KOH (1.961 g) was consumed by levulinic acid, the calculated quantity of which was 3.98 g (85.7%).

Study of polymers. By stepwise addition of methyl alcohol to a benzene solution containing 36.7 g of the polymer, 4 fractions were obtained, the analytical data for which are given in the table.

Physicochemical Constants of Polymeric Fractions

No. of fraction	Weight of fraction		Average molecular wt. (cryoscopic determination in benz.)		Total chlorine (in %)		Saponifiable chlorine (in %)		Calculated empirical formula
	in g	in %	found	calc.	found	calc.	found	calc.	
1	7.03	19.24	1345.2	1417	4.27	5.01	2.18	2.5	$C_{99}H_{158}Cl_2$
2	19.34	52.51	842.7	873	7.48	8.13	3.68	4.07	$C_{59}H_{88}Cl_2$
3	6.03	16.51	568.2	533	12.62	13.21	6.02	6.66	$C_{31}H_5Cl_2$
4	4.30	11.74							Mixture of dimers and trimers

2. Reaction of 1,3-Dichlorobutene-2 with Divinyl

In the presence of 0.25 g of $FeCl_3$ (0.75 mole%), 62.5 g of 1,3-dichlorobutene-2 and 13.8 g of divinyl were kept in a sealed ampoule in a nitrogen atmosphere at 20° for 20 hrs. The reaction product was washed with 10% hydrochloric acid and water in order to remove the catalyst, dried with $CaCl_2$, and then distilled. After the unreacted starting materials were driven off, the residue was distilled in vacuo. One fraction, b. p. 65-78° at 10 mm (4.1 g), and a residue (polymer, 5.8 g) were obtained thereby. By redistillation of this fraction, 2.75 g of product was obtained.

B. P. 74-76° at 10 mm, d^{20}_4 1.0737, $n^{20}D$ 1.4780, MR_D 47.22; calculated 47.94. Found %: Cl 39.2, sapon. Cl 19.6. M 167.0; bromine number 180.2. $C_8H_{12}Cl_2$. Calculated %: Cl 39.67, sapon. Cl 19.83. M 179; bromine number 181.

Corresponding fractions from several experiments were combined and ozonized. For ozonization 4.22 g of the product was taken. After decomposition of the ozonide with water and a 3% H_2O_2 solution the acid mixture did not contain formic acid (test with $AgNO_3$ solution).

After the volatile acids were distilled off in vacuo at 45-50° (35-40 mm), tarry crystals (3.5 g) remained in the flask. The hydrochloric acid in the volatile-acid mixture was determined from the chloride-ion content. There was found 0.51 g (60%) of HCl.

An aliquot part of the volatile-acid solution was treated with freshly precipitated silver oxide, the AgCl precipitate was filtered off, and the filtrate was evaporated in vacuo. The acetic acid was thereby isolated as the silver salt, which after recrystallization was analyzed.

Found %: Ag 63.84. $C_2H_3O_2Ag$. Calculated %: Ag 64.58.

No other acids were found in the form of the silver salts. For neutralization of the volatile acids, 1.74 g of KOH was required; of this the neutralization of hydrochloric acid used 0.784 g, and that of acetic acid used 0.956 g, which corresponds to 1.024 g (72.4%) of acetic acid.

The chloroacetic acid (b. p. 69-70° at 5 mm) was isolated from the crystalline residue by distillation in vacuo in the form of white crystals, m. p. 60-62°.

Found %: Cl 37.07. Equiv. 597.8. $C_2H_3O_2Cl$. Calculated %: Cl 37.56. Equiv. 592.6.

The quantity of chloroacetic acid was calculated from the chlorine content in the entire crystalline product (0.6 g), which corresponds to 1.6 g (71.8%) of chloroacetic acid.

The residual crystals from the distillation had m. p. 179-181° after recrystallization. For succinic acid, according to literature data, the m. p. is 182.3°. A mixture test with pure succinic acid gave no melting-point depression.

Found: equiv. 923.4. $C_4H_6O_4$. Calculated: equiv. 949.15.

The quantity of succinic acid was calculated from the total acidity of the aqueous solution. For neutralization 4.72 g of KOH was required; of this the neutralization of hydrochloric, acetic, and chloroacetic acids used 2.69 g; that of succinic acid (by difference) consumed 2.035 g of KOH, which corresponds to 2.145 g (75.24%) of succinic acid.

SUMMARY

1. The reaction of 1,3-dichlorobutene-2 with isoprene and divinyl in the presence of $FeCl_3$ has been investigated.

2. It has been found that in the reaction of 1,3-dichlorobutene-2 with isoprene and divinyl, both resinous substances of high molecular weight and primary addition products of low molecular weight are formed.

3. 1,7-Dichloro-3-methyloctadiene-2,6 – the product of addition of 1,3-dichlorobutene-2 to isoprene in the 1,4-position – has been isolated.

4. 1,7-Dichlorooctadiene-2,6 – the product of addition of 1,3-dichlorobutene-2 to divinyl in the 1,4-position – has been isolated.

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1,4-HYDROXYKETONES AND 1,4-DIKETONES IN THE CATALYTIC SYNTHESIS OF HOMOLOGS OF Δ^2-PYRROLINE AND Δ^2-DIHYDROTHIOPHENE, AND, CORRESPONDINGLY, HOMOLOGS OF PYRROLE AND THIOPHENE

Iu. K. Iur'ev and N. V. Makarov

In 1938 it was shown by one of us that on dehydration of butanediol-1,4 in the presence of alumina, furanidin (tetrahydrofuran) is formed, while on joint dehydration with ammonia and with hydrogen sulfide in the presence of alumina at 400°, pyrrolidine and thiophane, respectively, are obtained [1]; the joint catalytic dehydration of butanediol-1,4 with aniline in the presence of aluminosilicate at 330° [2] or activated alumina at 275° leads to N-phenylpyralidine.

It was also shown by one of us that the catalytic dehydration of cis-butene-2-diol-1,4 leads to Δ^3-dihydrofuran, while on joint catalytic dehydration of this diol and aniline in the presence of activated alumina at 350°, 1-phenyl-Δ^3-pyrroline is obtained [3]; similarly, on catalytic dehydration of butyne-2-diol-1,4, furan is obtained, while on joint catalytic dehydration with ammonia, with aniline, and with hydrogen sulfide at 400°, pyrrole, N-phenylpyrrole, and thiophene, respectively, are obtained [3].

The range of the reactions given above is widened by the latest instances of the catalytic dehydration of 1,4-diols of the types

$$RR'C(OH)C{=}CC(OH)R''R''';\quad RR'C(OH)CH{=}CHC(OH)R''R''',$$
$$RR'C(OH)CH_2{-}CH_2C(OH)R''R''',$$

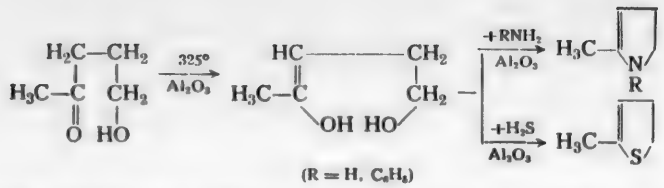
which leads to the formation of substituted furans, dihydrofurans, and furanidins, respectively [4], and also by instances of joint catalytic dehydration of the stated diols with ammonia and with alkyl- or arylamines with formation of N-substituted pyrroles, Δ^3-pyrrolines, or pyrrolidines, respectively [5-7]. Both alumina and alumina activated with various metal oxides were used as catalysts in these reactions [4-8].

Thus, into the catalytic synthesis of compounds with five-membered heterocyclic rings, both saturated and unsaturated 1,4-diols were introduced, the double or triple bond of the latter occupying a central position between the second and third carbon atoms in this system of four carbon atoms.

In connection with this, it was of interest to introduce into the described synthesis the simplest 1,4-hydroxyketone, and also the simplest 1,4-diketone, which on joint catalytic dehydration with ammonia, amines, or hydrogen sulfide must react in the enol forms as unsaturated diols with one and two hydroxyl groups, respectively, attached to doubly-bonded carbon atoms.

In the present work, as a representative 1,4-dihydroxyketone, we used γ-acetylpropyl alcohol, which, reacting in the enol form as pentene-2-diol-2,5, gave 2-methyl-Δ^2-pyrroline (50%) on treatment with ammonia in the presence of alumina at an elevated temperature, 1-phenyl-2-methyl-Δ^2-pyrroline (58%) on treatment with aniline, and 2-methyl-Δ^2-dihydrothiophene (38.5%) on treatment with hydrogen sulfide [9] (see diagram on next page).

Let us note that in the reaction with ammonia, increase in the rate of passage of γ-acetylpropyl alcohol over alumina from 0.45 to 0.8 ml/min and 1.6 ml/min led to decrease in the yield of 2-methyl-Δ^2-pyrroline and the appearance of ever-increasing quantities of 2-methyl-Δ^2-dihydrofuran. The latter resulted from the



(R = H, C_6H_5)

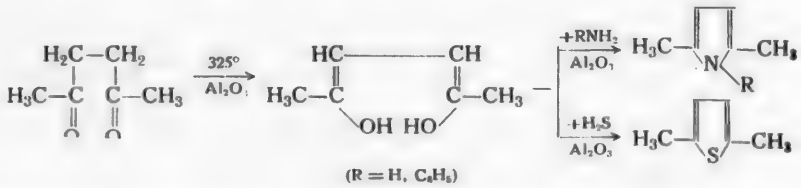
intramolecular catalytic dehydration of pentene-2-diol-1,4 – the enolization product of γ-acetylpropyl alcohol – which obviously proceeded at a higher rate than the joint catalytic dehydration with ammonia.

This also indicates that in the reactions described by us, elimination of water and closing of the nitrogen- or sulfur-containing ring take place directly through joint catalytic dehydration of ammonia, amines, or hydrogen sulfide and 1,4-diols, as well as 1,4-hydroxyketones (see below) in their enol forms.

Therefore, the formation of 2-methyldihydrofuran is not an obligatory intermediate stage in the catalytic synthesis of 2-methyl-Δ^2-pyrroline from γ-acetylpropyl alcohol and ammonia. With a definite reagent ratio and contact time the oxygen-containing heterocyclic compounds formed as by-products must be converted to the corresponding nitrogen-containing heterocyclic compounds by the reaction described by one of us [10], but at a lower rate, owing to the greater complexity of the process.

The joint catalytic dehydration of γ-acetylpropyl alcohol and aniline in the presence of aluminosilicate also led to 1-phenyl-2-methyl-Δ^2-pyrroline.

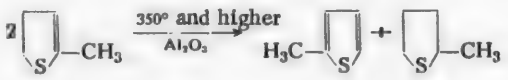
When acetonylacetone was introduced into the catalytic synthesis, we obtained 2,5-dimethylpyrrole (36%) on treatment with ammonia in the presence of alumina at an elevated temperature, 1-phenyl-2,5-dimethylpyrrole (43%) on treatment with aniline, and 2,5-dimethylthiophene (35%) on treatment with hydrogen sulfide [9].



(R = H, C_6H_5)

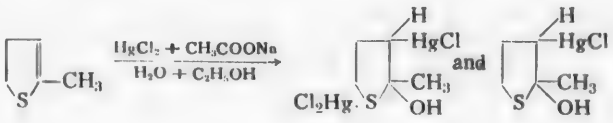
The preparation of this homolog in 35% yield by the joint catalytic dehydration of the 1,4-diketone (reacting in its enol form) and hydrogen sulfide shows how easily a reaction of this type occurs and how much simpler is the scheme which it follows, in comparison with the preparation of thiophene homologs by the catalytic conversion of furan homologs. In the latter case, on treatment of silvan with hydrogen sulfide in the presence of alumina, the yield of 2-methylthiophene did not exceed 10%, while 2,5-dimethylfuran, on treatment with hydrogen sulfide, was so strongly decomposed that only traces of 2,5-dimethylthiophene were obtained [11].

It should be particularly noted that the synthesis of 2-methyl-Δ^2-dihydrothiophene by the joint catalytic dehydration of γ-acetylpropyl alcohol and hydrogen sulfide goes relatively smoothly at 325° but by 350° appreciable amounts of 2-methylthiophene and 2-methylthiophane – products of the irreversible catalysis of 2-methyl-Δ^2-dihydrothiophene – appear in the reaction product together with the latter.



Thus we have obtained a direct proof of the fact that, like other incomplete hydrides of compounds of aromatic nature, dihydrothiophene and its homologs are subject to N. D. Zelinskii's irreversible catalysis [12]. This was first established by one of us in the study of the catalytic conversion of dihydrofuran under the influence of hydrogen sulfide, the product of which proved to be a mixture of thiophene and thiophane.

On mercuration of 2-methyl-Δ^2-dihydrothiophene by the Steinkopf method [14] – treatment with mercuric chloride in aqueous-alcoholic solution in the presence of sodium acetate – we obtained 1-dichloromercuri-2-methyl-2-hydroxy-3-chloromercurithiophane together with a small amount of 2-methyl-2-hydroxy-3-chloromercurithiophane.



EXPERIMENTAL

2-Methyl-Δ^2-pyrroline. Acetylpropyl alcohol was passed through a tube, filled with alumina (internal diameter of tube, 23 mm; length of catalyst layer, 40 cm), in a strong current of ammonia at a rate from 0.3 to 0.45 ml/min in the interval 275-350°.

The catalyzate obtained in the first receiver was saturated with solid potassium hydroxide and extracted with ether. In the second receiver, which was cooled with solid carbon dioxide and alcohol, the ammonia and the catalysis product, partly entrained by it, were condensed. After careful evaporation of the ammonia from a flask with a reflux condenser the residue was combined with the main mass of reaction product. After drying with potassium hydroxide and driving off the ether, the reaction products was distilled over sodium from a flask with a fractionating column, 2-methyl-Δ^2-dihydrofuran being collected at 79-82° and 2-methyl-Δ^2-pyrroline at 103-105°.

The results obtained in these experiments are given in Table 1.

TABLE 1

No. of expt.	Quantity of γ-acetylpropyl alcohol (in g)	Rate of introduction (ml/min)	Temperature of experiment	Yield of 2-methyl-Δ^2-pyrroline (in %)	Yield of 2-methyl-Δ^2-dihydrofuran (in %)
1	10.0	0.3	275°	12.0	—
2	10.0	0.3	300	18.5	—
3	10.0	0.3	325	24.0	—
4	10.0	0.3	350	18.5	—
5	10.0	0.35	325	38.0	—
6	10.0	0.45	325	50.0	—
7	18.0	0.8	325	18.5	16.0
8	18.0	1.6	325	10.5	31.0

From the data given in Table 1, it is evident that when acetylpropyl alcohol was introduced at a rate of 0.3 ml/min, the yield of 2-methyl-Δ^2-pyrroline increased from 12 to 24% as the reaction temperature rose from 275 to 325°, but decreased to 18.5% at 350°.

When the rate of introduction of the alcohol was increased to 0.45 ml/min at 325°, the yield of 2-methyl-Δ^2-pyrroline rose to 50%, but on further increase of the rate the yield of the latter fell, and ever-increasing amounts of 2-methyl-Δ^2-dihydrofuran appeared in the reaction product.

2-Methyl-Δ^2-pyrroline, combined from all experiments, after redistillation had the following constants:

B. p. 104-105° (756 mm), $n^{20}D$ 1.4356, d^{20}_4 0.8843, MR_D 26.00. C_5H_9N F. Calculated 26.18. Found %: C 72.54, 72.35; H 10.76, 10.86; N 16.91, 16.98. C_5H_9N. Calculated %: C 72.24; H 10.91; N 16.85.

2-Methyl-Δ^2-pyrroline picrate was obtained by mixing ethereal solutions of the base and of picric acid; m. p. 124°(from water).

Found %: N 17.80. $C_{11}H_{12}O_7N_4$. Calculated %: N 17.97. Literature data: b. p. 50-51° (110-116 mm), d^{22}_4 0.8995 [15], b. p. 90-91° (750 mm) [16], b. p. 105-110° [17].

The 2-methyl-Δ^2-dihydrofuran obtained in Experiments 7 and 8 was combined and redistilled over sodium:

B. p. 80-81° (750 mm), $n^{20}D$ 1.4089, d^{20}_4 0.8890, MR_D 22.70. C_5H_8O F. Calculated 22.83. Found %: C 71.31, 71.26; H 9.49, 9.53. C_5H_8O. Calculated %: C 71.39; H 9.58. Literature data: b. p. 75° [18], b. p. 82°, d^{20}_{20} 0.9062 [19].

1-Phenyl-2-methyl-Δ^2-pyrroline. Mixtures of γ-acetylpropyl alcohol and freshly distilled aniline in the molar ratios 1:1 and 1:2 were passed through a tube containing alumina (see above) at 330° and at rate of 0.3 to 0.6 ml/min in a slow current of nitrogen. The catalyzate obtained was saturated with potassium hydroxide and extracted with ether. After drying with potassium hydroxide and distilling off the ether and unchanged aniline (b. p. 48-49° at 1 mm), the reaction product — 1-phenyl-2-methyl-Δ^2-pyrroline — was collected at 85-87° (1 mm). The results obtained in these experiments are given in Table 2.

TABLE 2

No. of expt.	Quantity of acetylpropyl alcohol (in g)	Quantity of aniline (in g)	Molar ratio of reagents	Temperature of expt.	Rate of introduction of mixture (ml/min)	Yield of 1-phenyl-2-methyl-Δ^2-pyrroline (in %)
1	10.2	9.8	1 : 1	325°	0.4	24
2	10.2	19.6	1 : 2	330	0.4	52
3	5.2	9.8	1 : 2	330	0.3	58
4	5.2	9.8	1 : 2	330	0.5	50
5	5.2	9.8	1 : 2	330	0.6	45

From the data of Table 2, it is evident that the optimum conditions for preparing 1-phenyl-2-methyl-Δ^2-pyrroline (58% yield) are 330°, a molar ratio of acetylpropyl alcohol: aniline = 1 : 2 in the mixture and a rate of passage of the latter over the catalyst, equal to 0.3 ml/min.

1-Phenyl-2-methyl-Δ^2-pyrroline, after redistillation in a current of nitrogen, had the following constants:

B. p. 85-86° (2 mm), $n^{20}D$ 1.5762, d^{20}_4 1.0220, MR_D 45.67. $C_{11}H_{13}N$ F. Calculated 45.80. Found %: C 83.22, 83.37; H 8.46, 8.31; N 8.65, 8.62. $C_{11}H_{13}N$. Calculated %: C 83.00; H 8.24; N 8.79.

1-Phenyl-2-methyl-Δ^2-pyrolline picrate was obtained by mixing ethereal solutions of the base and of picric acid; m. p. 95° (from water).

Found %: N 14.46. $C_{17}HO_{16}O_7N_4$. Calculated %: N 14.40.

2-Methyl-Δ^2-dihydrothiophene. In each experiment 10 g of acetylpropyl alcohol was passed at a rate of 0.4 ml/min in a current of hydrogen sulfide through a tube filled with alumina (see above) and heated to 325°. The catalyzate was saturated with potassium hydroxide and extracted with ether. The other extract was dried with potassium hydroxide. After the ether was driven off, the residue was distilled over sodium from a flask with a fractionating column, a broad fraction being collected in the interval 105-135° at 756 mm (the main mass passed over at 128-129°); above 135°, obvious decomposition and resinification of the residue began.

TABLE 3

No. of fraction	Boiling point (743 mm)	Quantity (in ml)	n^{20}_D	d^{20}_4
1	105 —109.5°	4.3	1.4701	0.9545
2	109.5—128.5	3.3	1.5009	0.9877
3	128.5—129.5	12	1.5071	0.9906
4	129.5—130.5	16	1.5073	0.9900
5	130.5—131.5	2	1.5065	0.9847

In all, 6 experiments were conducted and 45 g of the stated fraction was obtained. On distillation of the latter through a column (18 theoretical plates), fractions were isolated, the constants of which are given in Table 3.

On redistillation of the third and fourth fractions, there was obtained 23 ml (22.8 g) (38.5%) of 2-methyl-Δ^2-dihydrothiophene:

B. p. 129-130° (745 mm), $n^{20}D$ 1.5073, d^{20}_4 0.9902, MR_D 29.83. C_5H_8S F. Calculated 29.45. Found %: C 59.95, 59.87; H 7.89, 7.94; S 31.87, 31.95. C_5H_8S. Calculated %: C 60.00; H 8.00; S 32.00.

On treatment of 1 g of 2-methyl-Δ^2-dihydrothiophene with a solution of 2.6 g of mercuric chloride and 3 g of sodium acetate in 80 ml of alcohol, diluted with 60 ml of water [14], 1-dichloromercuri-2-methyl-2-hydroxy-3-chloromercurithiophane was obtained; m. p. 143° (from alcohol).

Found %: Hg 64.00, 64.49. $C_5H_9OSCl_3Hg_2$. Calculated %: Hg 64.32.

Crystals of 2-methyl-2-hydroxy-3-chloromercurithiophane separated out from the mother liquor on standing.

Found %: Hg 56.42, 56.50. $C_5H_9OSClHg$. Calculated %: Hg 56.62.

Experiments on the catalytic synthesis of 2-methyl-Δ^2-dihydrothiophene from acetylpropyl alcohol (10 g in each experiment) were also conducted at 350°.

On distillation through a column (18 theoretical plates) of 6 g of the fraction with b. p. 105-135°, isolated from the catalyzates of two experiments of this series, besides 2-methyl-Δ^2-dihydrothiophene there were obtained:

a) 0.82 g of 2-methylthiophene; b. p. 110.5° (750 mm), $n^{20}D$ 1.5240, d^{20}_4 1.0200, MR_D 31.00. C_5H_6S F. Calculated 30.70. Literature data: b. p. 112-113°, $n^{20}D$ 1.5210, d^{20}_4 1.0168 [20].

By the mercuration of 2-methylthiophene, 2-methyl-5-chloromercurithiophene was obtained; m. p. 200° (from alcohol).

Found %: Hg 60.08. C_5H_5SClHg. Calculated %: Hg 60.18. Literature data: b. p. 197° [21], 202° [14].

b) 0.96 g of 2-methylthiophene; b. p. 131-132° (750 mm), $n^{20}D$ 1.4982, d^{20}_4 0.9577, MR_D 31.10. $C_5H_{10}S$. Calculated 31.30. Literature data: b. p. 131.2-132° (756 mm), $n^{20}D$ 1.4922, d^{20}_4 0.9577 [22].

2,5-Dimethylpyrrole. In each experiment 10 g of acetonylacetone was passed over alumina at 325° at a rate of 0.4 ml/min in a strong current of ammonia. After the appropriate treatment of the catalyzates from two experiments and distillation of the reaction product, there was obtained 6 g (36%) of 2,5-dimethylpyrrole:

B. p. 165-166° (759 mm), $n^{20}D$ 1.5028, d^{20}_4 0.9288, MR_D 30.25. C_6H_9N F. Calculated 30.37. Found %: N 14.84, 14.89. C_6H_9N. Calculated %: N 14.73.

At 350° the yield of 2,5-dimethylpyrrole fell to 30%.

Literature data: b. p. 165° (740 mm) [23], 166.5 (756 mm), $n^{19.8}D$ 1.5036, $d^{19.8}_4$ 0.9353 [24]; b. p. 170-172° (765 mm), $n^{20}D$ 1.5028, d^{20}_4 0.9344 [25].

1-Phenyl-2,5-dimethylpyrrole. A mixture of 6 g of acetonylacetone and 9.5 g of aniline (molar ratio 1:2) was passed over alumina at 325° at a rate of 0.35 ml/min in a slow current of nitrogen. After the appropriate treatment of the catalyzates from two experiments and distillation of the reaction product, there was obtained 13 g (43%) of 1-phenyl-2,5-dimethylpyrrole; m. p. 52-52.5°.

Found %: N 8.25, 8.29. $C_{12}H_{13}N$. Calculated %: N 8.18. Literature data: b. p. 252°, m. p. 51-52° [26]; m. p. 52-53° [25].

2,5-Dimethylthiophene. Acetonylacetone was passed over alumina at a rate of 0.4 ml/min in a strong current of hydrogen sulfide at 275, 325, and 350°. The catalyzate was treated as described under 2-methyl-Δ^2-dihydrothiophene. On distillation of the catalysis product, 2,5-dimethylthiophene was collected at 133-135°. The results obtained in these experiments are given in Table 4.

After redistillation of all the 2,5-dimethylthiophene over sodium, it had the following constants:

B. p. 134-135° (759 mm), $n^{20}D$ 1.5045, d^{20}_4 0.9775, MR_D 43.61. C_6H_8S F. Calculated 43.52. Found %: C 64.09, 64.17; H 7.21, 7.10; S 28.49, 28.47. C_6H_8S. Calculated %: C 64.23; H 7.18; S 28.57. Literature

TABLE 4

No. of expt.	Quantity of acetonylacetone (in g)	Temperature of expt.	Rate of introduction (ml/min)	Yield of 2,5-dimethylthiophene, %	n_D^{20}	d_4^{20}
1	10	275°	0.4	16.5	1.5046	0.9780
2	10	325	0.4	35.0	1.5040	0.9778
3	10	350	0.4	33.0	1.5043	0.9775

data: b. p. 134-135°, d^{19}_4 0.9755 [27], b. p. 136.5-137.3°, $d^{17.5}$ 0.9755 [28]; b. p. 135.5-136° (754.3 mm), $n^{19}D$ 1.51418, d^{19}_4 0.9858 [24].

2,5-Dimethyl-3-chloromercurithiophene melted at 187°.

Found %: Hg 57.69. C_6H_7SClHg. Calculated %: Hg 57.77. Literature data: b. p. 186° [14].

SUMMARY

1,4-Hydroxyketones and 1,4-diketones may well be used in the catalytic synthesis of heterocyclic compounds having a five-membered nitrogen- or sulfur-containing nucleus; the joint catalytic dehydration of γ-acetylpropyl alcohol with ammonia, with aniline, and with hydrogen sulfide in the presence of alumina at 325-330° is a good method of synthesis of 2-methyl-Δ^2-pyrroline, 1-phenyl-2-methyl-Δ^2-pyrroline, and 2-methyl-Δ^2-dihydrothiophene, respectively; on joint catalytic dehydration of acetonylacetone with ammonia, with aniline and with hydrogen sulfide in the presence of alumina at 325°, 2,5-dimethylpyrrole, 1-phenyl-2,5-dimethylpyrrole, and 2,5-dimethylthiophene, respectively, are obtained.

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HETEROCYCLIC DERIVATIVES OF METHYL KETONES

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Many nitrogen heterocyclics containing a methyl group adjacent to the nitrogen atom readily undergo electrophilic substitution reactions. This is also true in condensation with esters.

In 1898 Wislicenus [1] condensed oxalic ester with quinaldine to prepare a substituted ester of pyruvic acid. Later on this reaction was studied in more detail by Borsche et al. [2], who extended it to other heterocyclics [3]. Diethyl oxalate is one of the most active acylating esters in condensations of this type. It seemed interesting to study this condensation with less active components also, such as ethyl benzoate and other esters.

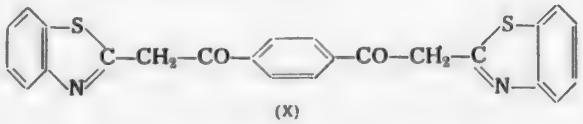
In the presence of potassium ethoxide, ethyl benzoate reacts with 2-methyl homologs of various heterocyclics to form ketones by the scheme

(I) X = S, R = C_6H_5; (II) X = O, R = C_6H_5; (III) X = Se, R = C_6H_5; (IV) X = CH = CH, R = C_6H_5; (V) X = = NCH_3, R = C_6H_5; (VI) X = S, R = CH_3; (VII) X = S, R = p-$CH_3OC_6H_4$; (VIII) X = S, R = p-ClC_6H_4; (IX) X = S, R = p-$C_2H_5OCOC_6H_4$.

2-Methylbenzimidazole is an exception and does not react at all under these conditions. The yield of ketone obtained varies from 5 to 28% depending on the part of the heterocyclic X. If the various possibilities for the latter are arranged according to the increasing activity of the heterocyclic, we obtain the following series: NH < Se < NCH_3 < CH = CH < O < S, which agrees in general with the order of the decreasing basicity of the corresponding heterocyclics, determined from their other properties [4]. Benzselenazole is an exception, but this may be explained by the presence of side reactions during its condensation with ethyl benzoate.

One of the ketones which we prepared, ω-benzoyl-2-methylbenzthiazole (I), was described previously by Rogers and Sexton, who prepared it by another method [5].*

Para-substituted ethyl benzoates were noticeably more active in the reaction with 2-methylbenzthiazole. Thus, ethyl p-methoxybenzoate formed the corresponding ketone (VII) in 45% yield, ethyl p-chlorobenzoate gave 56% of (VIII) and diethyl terephthalate a 79% yield. In the latter case, about 2% of the diketone (X) was formed in addition to ω-(p-carbethoxybenzoyl)-2-methylbenzthiazole (IX).



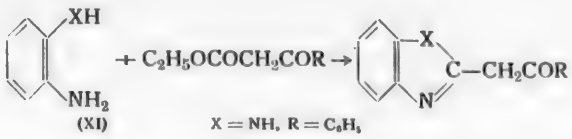
(X)

The ketoester (IX) may be readily hydrolyzed to form the corresponding acid.

Ethyl acetate is less active in a condensation with 2-methylbenzthiazole and the reaction yielded only about 3% of ω-acetyl-2-methylbenzthiazole; the bulk (85%) of the 2-methylbenzthiazole used was recovered unchanged.

* In the work cited, the m. p. of 150° was attributed to this substance mistakenly, instead of the true value, 110-111°.

The same heterocyclic ketones, with the exception of (IV), may be prepared by other methods – the condensation of o-substituted anilines with acyl- or arylacetic esters by the scheme

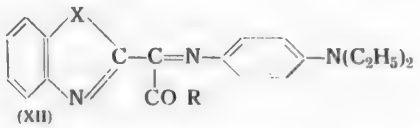


(XI) X = NH, R = C_6H_5

This scheme was described by Sexton [6] for the preparation of ω-acetyl-2-methylbenzimidazole and in a general form by Wilson [7].

In this way we prepared ω-benzoyl-2-methylbenzimidazole (XI), which was not obtained in the ester condensation; a series of other ketones of this type were also prepared for a comparison of the preparative methods.

The heterocyclic ketones synthesized had active methylene groups between the heterocyclic and the carbonyl. This activity was illustrated by condensation with aldehydes and the formation of azomethine dyes (XII)



(XII)

in an oxidative condensation with dialkyl-p-phenylenediamines. These ketones gave an intense green color with ferric chloride solution; the exceptions were ω-benzoylquinaldine, which has low activity, and the completely inactive ω-benzoyl-2-methylbenzimidazole.

EXPERIMENTAL

ω-Benzoyl-2-methylbenzithiazole (I). 7.5 g of ethyl benzoate and 7.5 g of 2-methylbenzthiazole were added to a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The mixture was heated in a flask with a small column for 4 hrs, while the azeotropic mixture of benzene and the alcohol formed was slowly distilled off. 2N acetic acid was added to the thick, orange mass formed until the precipitate dissolved completely and the benzene layer was separated, washed with 5% bicarbonate solution and dried with sodium sulfate. After removal of the solvent and unreacted starting materials at up to 104° (9 mm), the residue crystallized. The substance weighed 3.5 g (27.7%) after being washed with methanol; the yellow prisms (from methanol) had m. p. 110-111°. A mixture with the substance prepared according to the data in [5] melted at 110°.

Found %: C 71.06; H 4.43; N 5.74; S 12.64. $C_{15}H_{11}ONS$. Calculated %: C 71.11; H 4.38; N 5.53; S 12.66.

ω-Benzoyl-2-methylbenzoxazole (II) was prepared from 7.5 g of ethyl benzoate, 6.65 g of 2-methylbenzoxazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 2.5 g (21.5%); the greenish needles (from aqueous methanol) melted at 88-88.5°.

Found %: C 76.06; H 4.49; N 6.13. $C_{15}H_{11}O_2N$. Calculated %: C 75.97; H 4.67; N 5.90.

ω-Benzoyl-2-methylbenzselenazole (III) was prepared from 7.5 g of ethyl benzoate, 9.8 g of 2-methylbenzselenazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 0.79 g (5.3%); the yellow prisms (from aqueous methanol) had m. p. 186.5-187°.

Found %: C 59.73; H 3.68; N 4.59. $C_{15}H_{11}ONSe$. Calculated %: C 60.01; H 3.69; N 4.66.

ω-Benzoylquinaldine (IV) was prepared from 7.5 g of ethyl benzoate, 7.15 g of quinaldine and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 1.4 g (11.3%); the bright orange prisms (from methanol) had m. p. 114-115°.

Found %: C 82.51; H 5.46; N 5.70. $C_{17}H_{13}ON$. Calculated %: C 82.57; H 5.03; N 5.67.

ω-Benzoyl-1,2-dimethylbenzimidazole (V) was prepared from 7.5 g of ethyl benzoate, 7.3 g of 1,2-dimethylbenzimidazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 1.08 g (8.6%); the light yellow needles (from methanol) had m. p. 151-151.5°.

Found %: C 77.08; H 5.68; N 11.38. $C_{16}H_{14}ON_2$. Calculated %: C 76.78; H 5.59; N 11.11.

ω-Acetyl-2-methylbenzthiazole (VI). a) 4.4 g of ethyl acetate and 7.5 g of 2-methylbenzthiazole were added to a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The mixture was heated under reflux for 24 hrs. The precipitate, which formed on cooling, was treated similarly to (I). The yield was 0.26 g (2.7%); the light yellow prisms (from methanol) had m. p. 116-116.5°.

b) The substance was prepared similarly to (I) from 6.25 g of o-aminothiophenol and 7.8 g of ethyl acetoacetate in 70 ml of xylene. The yield was 4.43 g (46.3%); the light yellow prisms (from methane) had m. p. 116-117°; a mixture with the substance obtained by method (a) melted at 116°.

Found %: C 62.96; H 4.75; N 7.38; S 16.59. $C_{10}H_9ONS$. Calculated %: C 62.80; H 4.74; N 7.32; S 16.77.

ω-(p-Methoxybenzoyl)-2-methylbenzthiazole (VII). a) The substance was prepared from 9.0 g of ethyl p-methoxybenzoate, 7.5 g of 2-methylbenzthiazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 6.36 g (44.9%); the yellow needles (from xylene) had m. p. 114-114.5°.

b) The substance was prepared similarly to (I) from 6.25 g of o-aminothiophenol and 11.1 g of ethyl p-methoxybenzoylacetate in 70 ml of xylene. The yield was 12.4 g (87.5%); the needles (from xylene) had m. p. 114-115°; a mixture with the substance obtained by method (a) melted at 114°.

Found %: C 67.98; H 4.59; N 5.04; S 11.31. $C_{16}H_{13}O_2NS$. Calculated %: C 67.82; H 4.62; N 4.94; S 11.32.

ω-(p-Chlorobenzoyl)-2-methylbenzthiazole (VIII) was prepared from 9.23 g of ethyl p-chlorobenzoate, 7.5 g of 2-methylbenzthiazole and a suspension of 5 g of potassium ethoxide in 50 ml of benzene. The yield was 8.02 g (55.7%); the yellow needles (from xylene) had m. p. 141-142°.

Found %: C 62.47; H 3.58; N 4.88; S 11.06; Cl 12.56. $C_{15}H_{10}ONSCl$. Calculated %: C 62.60; H 3.49; N 4.87; S 11.14; Cl 12.32.

ω-(p-Carbethoxybenzoyl)-2-methylbenzthiazole (IX) was prepared from 11.1 g of diethyl terephthalate, 14.9 g of 2-methylbenzthiazole and a suspension of 10 g of potassium ethoxide in benzene. The yield was 12.85 g (78.9%); the yellow needles (from glacial acetic acid) had m. p. 150.5-151.5°.

Found %: C 66.24; H 4.59; N 4.65; S 10.08. M 305.81 (per Rast). $C_{18}H_{15}O_3NS$. Calculated %: C 66.44; H 4.65; N 4.35; S 9.86. M 325.37.

ω-(p-Carboxybenzoyl)-2-methylbenzthiazole. 1 g of (IX) was dissolved in 20 ml of 5% alcohol solution of sodium hydroxide in the cold. The precipitate which formed after a short time (0.93 g) was dissolved in 100 ml of water and made weakly acid with 0.5 N hydrochloric acid. The weight of the precipitate was 0.83 g (90.9%); the yellow plates (from glacial acetic acid) had m. p. 251.5-252.2°.

Found %: C 64.32; H 3.76; N 4.72; S 10.96. M 263.38 (titration with alkali). $C_{16}H_{11}O_3NS$. Calculated %: C 64.63; H 3.73; N 4.71; S 10.78. M 297.32.

ω-Terephthaloyl-bis-(2-methylbenzthiazole) (X). a) After the recrystallization of (IX) from glacial acetic acid, an insoluble precipitate remained, which weighed 0.36 g (1.68%). The yellow plates (from chlorobenzene) had m. p. 255-256°.

b) The substance was prepared from 5.0 g of o-aminothiophenol and 6.12 g of terephthaloylbisacetic ester in 70 ml of xylene. The yield was 6.65 g (77.6%); the plates (from chlorobenzene) had m. p. 255-256°; a mixture with the substance prepared by method (a) melted at 255°.

Found %: C 67.56; H 3.74; N 6.58; S 15.03. $C_{24}H_{16}O_2N_2S_2$. Calculated %: C 67.27; H 3.76; N 6.54; S 14.97.

ω-Benzoyl-2-methylbenzimidazole (XI). The substance was prepared from 5.4 g of o-phenylenediamine and 9.6 g of ethyl benzoylacetate in 100 ml of xylene. The yield was 9.65 g (81.8%); the white needles (from methanol) had m. p. 195-195.5°.

Found %: C 76.23; H 5.26; N 11.89. $C_{15}H_{12}ON_2$. Calculated %: C 76.25; H 5.24; N 11.87.

ω-(p-Nitrobenzoyl)-2-methylbenzthiazole. The substance was prepared from 2.5 g of o-aminothiophenol and 4.77 g of p-nitrobenzoylacetic ester in 100 ml of dry benzene. The yield was 0.92 g (15.4%); the yellow needles (from benzene) had m. p. 211.5-212.5°.

Found %: C 60.33; H 3.34; N 9.19; S 10.88. $C_{15}H_{10}O_3N_2S$. Calculated %: C 60.39; H 3.38; N 9.39; S 10.75.

ω-Stearoyl-2-methylbenzthiazole. The substance was prepared from 2.5 g of o-aminothiophenol and 7.1 g of stearoylacetic ester in 50 ml of xylene. The yield was 3.0 g (36.1%); the white prisms (from methanol) had m. p. 59.5-60.5°.

Found %: C 75.08; H 9.73; N 3.61; S 7.81. $C_{26}H_{41}ONS$. Calculated %: C 75.12; H 9.94; N 3.37; S 7.71.

Properties of Azomethine Dyes

Heterocyclic ketone	Yield of dye (in %)	External appearance, melting point and absorption maximum in alcohol	Nitrogen content (in %)		Formula of dye
			found	calc.	
ω-Benzoyl-2-methylbenzthiazole	69.5	Orange prisms, 236-237°, 462 mμ	10.20	10.16	$C_{25}H_{23}ON_3S$
ω-Benzoyl-2-methylbenzoxazole	45.6	Orange prisms, 197-198°, 462 mμ	10.30	10.56	$C_{25}H_{23}O_2N_3$
ω-Benzoyl-2,3-dimethylbenzimidazole	32.9	Brown prisms, 174-175° (with darkening), 445 mμ	13.81	13.65	$C_{26}H_{26}ON_4$
ω-Acetyl-2-methylbenzthiazole	69.7	Red prisms, 136-137°, 450 mμ	12.80	12.99	$C_{18}H_{17}ON_3S$
ω-(p-Methoxybenzoyl)-2-methylbenzthiazole	55.7	Orange prisms, 178-179°, 460 mμ	9.38	9.48	$C_{26}H_{25}O_2N_3S$
ω-(p-Chlorobenzoyl)-2-methylbenzthiazole	76.4	Orange prisms, 164-165°, 465 mμ	9.99	9.38	$C_{25}H_{22}ON_3SCl$
ω-(p-Carbethoxybenzoyl)-2-methylbenzthiazole	36.1	Red prisms, 214-215°, 450 mμ	8.94	8.65	$C_{28}H_{27}O_3N_3S$
ω-(p-Carboxybenzoyl)-2-methylbenzthiazole	71.4	Orange prisms, 145-146°, 462 mμ	9.42	9.19	$C_{25}H_{23}O_3N_3S$
ω-Terephthaloyl-bis(2-methylbenzthiazole)	57.7	Brown prisms, 225-226°	9.79	9.52	$C_{34}H_{28}O_2N_4S_2$

Benzal derivative of ω-benzoyl-2-methylbenzthiazole. A solution of 1.26 g of ω-benzoyl-2-methylbenzthiazole and 1.06 g of benzaldehyde in 60 ml of pyridine with 3 drops of piperidine was boiled under reflux for 2 hrs. After cooling, it was poured into 5% sulfuric acid solution (weakly acid reaction). The oily precipitate formed solidified into a yellow crystalline mass. The weight of the benzoyl derivative was 1.2 g (70.3%); the prisms (from glacial acetic acid) had m. p. 119-119.5°.

Found %: C 77.24; H 4.50; N 4.41; S 9.28. $C_{11}H_{15}ONS$. Calculated %: C 77.39; H 4.46; N 4.10; S 9.39.

Azomethine dyes (XII). A suspension of equimolecular amounts of ketone and p-nitrosodiethylaniline * in 30 ml of anhydrous alcohol with 3 drops of piperidine was boiled under reflux on a water bath for half an hour. The cooled solution deposited a precipitate of the dye, which was recrystallized from alcohol (table).

* For the condensation with ω-acetyl-2-methylbenzthiazole, p-nitrosodimethylaniline was used.

SUMMARY

2-Methyl homologs of many nitrogen heterocyclics condense with esters, forming ketones. These ketones are formed in higher yields by condensing ortho-substituted anilines with β-ketoesters. The heterocyclic ketones obtained by these reactions possess an active methylene group.

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SYNTHESIS AND REACTIONS OF SOME THIAZOLIDINE DERIVATIVES

1. PREPARATION OF AZORHODANINES

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Rhodanine (2-thionethiazolidone-4) is one of the most important representatives of the thiazolidines, which are especially interesting compounds in connection with the proof of the structure of penicillin, whose molecule is based on a thiazolidine ring. Rhodanine reacts readily with a series of other compounds due to its characteristically labile hydrogen atoms at position five [1].

Aldehydes [1], quinones [2], nitroso compounds [2, 3], ketones [4] and more complex oxo compounds [5] condense with rhodanine. The various rhodanine derivatives obtained by this method, have been used in a variety of ways, mainly in analytical chemistry. As Feigl [6], Kolthoff [7], Kuznetsov [8] and others have shown in their work, some rhodanines may be used as extremely sensitive reagents, which precipitate silver, mercury and copper from solutions of their salts. Starting with rhodanine, merocyanin dyes may be synthesized [9] and these are used as photosensitizers. Hydrolysis of the condensation products of aldehydes and rhodanine gives thiopyroracemic acids, which can then be readily converted to amino acids, nitriles, amines and other substances. It should be noted that the interest in rhodanines has been increasing recently as their fungicide [10, 11], goitrogenic and antithyroid properties [12] have been established and this has stimulated the study of various syntheses of rhodanine derivatives.

In studying the reactions of rhodanine with certain compounds, we became interested in the possibility of coupling such active materials as diazonium salts with rhodanine. It is known that the former will couple not only with amines and phenols, but also with other compounds with labile hydrogen atoms, such as for example, with pyrazolone derivatives, benzoylacetone, the anilide of acetoacetic acid, sulfazone, oxindole and others [13]. Recently diazotized sulfanilamide was successfully azo-coupled with 2-arylamino-4-thiazolidone [14]; however, there is no data in the literature on the reaction of rhodanine with diazonium salts. The syntheses we carried out in this direction gave a series of new compounds, azorhodanines, with the general formula $R-N=N-CH(-S-)-CO-NHCS$, where R = aryl (table).

The substances obtained may be not only of theoretical but also of practical interest as new azo dyes. In addition, since therapeutically valuable amines were used in these syntheses, one would expect the formation of new physiologically active preparations. In this case one should take into account the fact that the introduction of a thiazolidine ring into the molecule of a substance usually results in a decrease in its toxicity [15]. Rhodanine, which has acid properties, may be compared with phenols in its role of an azo component and we therefore decided to carry out the coupling in an alkaline medium. However, rhodanine is extremely unstable in solutions of caustic alkali and even in the cold it was rapidly and completely hydrolyzed to form thioglycolic and thiocyanic acids [16]. We therefore used a weak, 3-3.5% solution of ammonia in an amount sufficient to maintain a weakly ammoniacal medium till the end of the reaction. Under these conditions at low temperature and with rapid coupling, rhodanine was hardly hydrolyzed and the bulk of the product formed was precipitated. An increase in the ammonia concentration resulted in decomposition of the diazo compound and hydrolysis and solution of the reaction product which complicated its isolation and lowered the yield. The azorhodanines which did not precipitate were isolated from the reaction solution by salting out with sodium chloride or by acidifying.

Properties of Azorhodanines with the General Formula R N=N CH CO NH CS (S)

R	Color	Melting pt. (decomp.)	Yield (in %)	Color change range (pH)	Content (in %) found	Content (in %) calc.
C_6H_5	Yellow-orange	234—236° (decomp.)	98	10.0—11.5	N 17.75, S 26.85	N 17.71, S 27.02
p-$CH_3C_6H_4$	Orange	226—228 (decomp.)	94	7.5—11.1	N 16.65, S 25.50	N 16.71, S 25.51
$C_6H_4OCH_3$-o	Crimson	215—216 (decomp.)	95	—	N 15.90	N 15.71
$C_6H_4OCH_3$-	Brick red	188—190	97	8.8—11.4	N 15.54	N 15.71
$(CH_3)_2NC_6H_4$	Brown	125 (decomp.)	96	7.6—11.0	N 19.68	N 19.98
$(C_2H_5)_2NC_6H_4$	Brown	132—134 (decomp.)	97	8.7—11.8	N 17.56	N 18.16
$C_6H_4OC_2H_5$-p	Red-orange	207—209	91	—	N 14.84	N 14.93
C_6H_4COOH-o	Yellow	248—249 (decomp.)	91	—	N 14.89, S 22.60	N 14.93 S 22.77

The substances obtained were shown to be azo compounds by analytical determinations and by reduction which gave the original amines and breakdown products of the rhodanine ring. The materials obtained were proved to be 5-substituted rhodanines by the following: a) all the azorhodanines synthesized dissolved readily in alkalis with very intense coloring, i. e., they have acid properties while N-substituted rhodanines are neutral and insoluble in alkaline solutions; b) alkaline hydrolysis of the azorhodanines resulted in the formation of thiocyanic acid and the corresponding α-substituted thioketo acids; c) 5-substituted rhodanines, for example, 5-isopropylidenerhodanine, are incapable of combining with diazonium salts; and d) azorhodanines do not react with aldehydes.

Regarding possible isomeric forms, as our preliminary investigations showed, a hydrazone structure should be assigned to the materials obtained as this is confirmed by: a) the easy reduction of azorhodanines to amines with zinc dust in an alkaline medium; b) their solubility in concentrated sulfuric acid with intense coloring, which may be explained by weakly basic properties resulting from the imine nitrogen of the −NH−N= group; c) formation by hydrolysis of hydrazothioketo acids with the structure R·NH·NHCSCOOH.

Azorhodanines are yellow, orange, red and more rarely, brown, in color with various shades. Their solutions change color very readily over a narrow pH range in going from an acid to an alkaline medium, i. e., behave as indicators. Azorhodanines are very sensitive reagents for silver, copper and mercury salts with which they form characteristically colored precipitates.

EXPERIMENTAL

5-(Phenylazo)-rhodanine (I). 4.65 g of aniline was added to a mixture of 12.5 ml of concentrated hydrochloric acid and 25 ml of water and diazotized with a solution of 3.75 g of sodium nitrite in 15 ml of water, while cooled with ice. After half an hour, a solution of 7 g of rhodanine in a mixture of 14 ml of 25% ammonia, 70 ml of water and 30 g of ice was prepared. The diazo solution was rapidly added to the solution obtained from a dropping funnel (with vigorous stirring and cooling). A yellow-orange color was immediately produced and then a suspension of a precipitate formed. After being mixed for half an hour, the reaction mixture was left for 1 hr in the cold, then the precipitated reaction product was filtered off, washed with warm dilute acid and dried. The yield was 23.2 g (98%). The crude product was dissolved in a warm 5% soda solution and precipitated with hydrochloric acid. On recrystallization from 75% alcohol, it formed right-angled yellow-orange

plates with m. p. 234-236° (decomp.). It was readily soluble in methyl and ethyl alcohols, dioxane, acetone, ethyl acetate, acetic acid and aniline, difficultly soluble in ether, benzene, and xylene and insoluble in water. Solutions in alkalis had an intense red-orange color and in concentrated sulfuric acid, cherry red. A change in color from greenish yellow to pink occurred in the pH range 10.0-11.5. Aqueous alcohol solutions gave precipitates with copper, silver and mercury salts, which were brownish red, red-violet and yellow-brown, respectively in color.

Found %: N 17.75; S 26.85. $C_9H_7ON_3S_2$. Calculated %: N 17.71; S 27.02.

Reduction of (I). 0.3 g of (I) was dissolved in 15 ml of 8% NaOH and zinc dust added. Gentle heating produced complete decolorization of the solution and the simultaneous evolution of ammonia. The solution was filtered. The presence of aniline and thiocyanate ions in the solution was demonstrated by qualitative reactions.

5-(4'-Methylphenylazo)-rhodanine (II). This was prepared similarly to (I) by the diazotization of 5.4 g of p-toluidine and coupling with 7 g of rhodanine, dissolved in a mixture of 15 ml of ammonia and 80 ml of water at −2°. It formed fine orange needle-like crystals. The yield was 11.8 g (94%). It crystallized from nitrobenzene as an orange powder, decomposing at 226-228°. The product was readily soluble in most organic solvents and especially in dioxane. Solutions in alkalis were orange-red and in concentrated sulfuric acid, cherry-violet. When reduced it gave p-toluidine. A change in color from light yellow to lilac occurred in the pH range 7.5-11.1.

Found %: N 16.65; S 25.50. $C_{10}H_9ON_3S_2$. Calculated %: N 16.71; S 25.51.

5-(2'-Methoxyphenylazo)-rhodanine (III). This was formed by coupling 6.15 g of diazotized o-anisidine with 7 g of rhodanine in 110 ml of 3.5% ammonia and subsequent salting out with sodium chloride. The yield was 12.7 g (95%). The orange powder was slightly soluble in hot water and readily soluble in alcohol, dioxane, acetone and ethyl acetoacetate. From acetic acid it formed crimson red needles with m. p. 215-216° (decomp.). The substance could also be recrystallized from butanol, isoamyl alcohol and m-xylene. Alkaline solutions were bright red in color. The material dissolved in concentrated sulfuric acid to give an intense violet color, which disappeared on dilution with water.

Found %: N 15.90. $C_{10}H_9O_2N_3S_2$. Calculated %: N 15.71.

5-(4'-Methoxyphenylazo)-rhodanine (IV). This substance was prepared similarly to (III) from the diazo compound of p-anisidine and rhodanine. Salting out was not required. The yield was 13.0 g (97%). The substance formed a red powder. It was insoluble in water, readily soluble in alcohols and other organic solvents and very readily soluble in pyridine. Three reprecipitations from dioxane with water gave red-orange needles with m. p. 188-190° (decomp.). Solutions in alkalis were bright red and in concentrated sulfuric acid, violet. A change in color from light yellow to orange-pink occurred in the pH range 8.8 to 11.4.

Found %: N 15.54. $C_{10}H_9O_2N_3S_2$. Calculated %: N 15.72.

5-(4'-Dimethylaminophenylazo)-rhodanine (V). This compound was prepared similarly to (III) from 3.0 g of rhodanine in 40 ml of 3.5% ammonia and diazotized p-dimethylaminoaniline. The yield was 5.2 g (96%). The dark brown powder was soluble in acids, alkalis and the bulk of organic solvents. Solutions in chloroform, benzene, aniline and nitrobenzene, in contrast to others, had an extremely intense cherry red color. Precipitation from ethanol with water gave fine needles, decomposing at 125°. A change in color from yellow-brown to lilac occurred in the pH range from 7.6-11.0.

Found %: N 19.68. $C_{11}H_{12}ON_4S_2$. Calculated %: N 19.98.

5-(4'-Diethylaminophenylazo)-rhodanine (VI). This substance was prepared in 97% yield (15 g) by reacting diazotized p-diethylaminoaniline sulfate (12.5 g) with 7.5 g of rhodanine in 100 ml of 3.5% ammonia. Coupling was accompanied by slight foaming. The reaction mixture was kept for 12 hrs in ice and water, then the dye was filtered off and air dried. The dark red, finely crystalline powder decomposed at 131-133°. It was similar to (V) in solubility. There was a noticeable color change in the pH range 8.7-11.8.

Found %: N 17.56. $C_{13}H_{16}ON_4S_2$. Calculated %: N 18.17.

5-(4'-Ethoxyphenylazo)-rhodanine (VII). 17.4 g of p-phenetedine hydrochloride was diazotized and coupled at −5 to 0° with 15.0 g of rhodanine in 28 ml of ammonia, 80 ml of water and 50 g of ice. The diazo solution was added over a period of 20 min. After 12 hrs, the dye was filtered off and washed with water. Part of the dye precipitated from the diluted mother liquor. The total yield was 26 g (91%). The red powder, consisting of fine needles, was readily soluble in methanol and ethanol and difficultly soluble in ether, benzene and chloroform; it dissolved with heating in acetone, dioxane, xylene and ethyl acetoacetate; it was insoluble in water. It crystallized from acetic acid as red-orange needles with m. p. 207-209°. A solution in concentrated sulfuric acid was intense violet and an alkaline solution, bright red.

Found %: N 14.84. $C_{11}H_{11}O_2N_3S_2$. Calculated %: N 14.93.

5-(2'-Carboxyphenylazo)-rhodanine (VIII). 3.45 g of anthranilic acid was diazotized and coupled at 0° with 3.8 g of rhodanine in 9.5 ml of ammonia and 40 ml of water. After 2 hrs, 10 g of sodium chloride was added and after a further 1 hr, the precipitated dye was filtered off and carefully washed with cold water. The red-orange powder became deeper in color on heating. The yield was 13 g (91%). The product crystallized from 93% alcohol, acidified with hydrochloric acid, as light yellow needles, which were readily soluble in dioxane, in water and alcohol on heating and slightly soluble in ether. The m. p. was 248-249° (decomp.). The substance gave yellow precipitates with salts of iron, lead, cobalt and cadmium. The sensitivity of the reaction with silver salts made it possible to determine the solubility of metallic silver in water.

Found %: S 22.60; N 14.89. $C_{10}H_7O_3N_3S_2$. Calculated %: S 22.77; N 14.93.

SUMMARY

Synthesis conditions are proposed for compounds of diazonium salts with rhodanine which were previously unknown; 8 new substances, azorhodanines, were prepared and are described. The materials synthesized have acid properties and are 5-arylazo substituted rhodanines.

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INVESTIGATION OF THE CHEMISTRY OF ORGANIC OXIDES

XIV. REACTION OF THE α-OXIDE OF ISOPRENE WITH AMMONIA AND AMINES

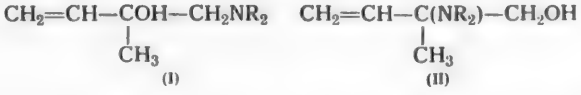
V. M. Al'bitskaia and A. A. Petrov

In a previous report we characterized the hydroxyamines formed by reacting divinyl oxide with primary and secondary amines [1]. The present paper describes the results of our experiments on the reactions of isoprene α-oxide (1,2-epoxy-2-methylbutene-3) with ammonia and amines. We could find no data on this problem in the literature.

By adding ammonia and four primary (from methyl-to butylamine) and four secondary (from dimethylamine to dibutylamine) amines to isoprene oxide, 9 amine alcohols were prepared with the constants given in the table. A comparison of the constants of these substances with those of the products obtained under similar conditions from divinyl oxide shows the considerably lower boiling points of the former, which are remarkable as these substances have an extra methyl group. The boiling points rise, the specific gravities decrease and the refractive indexes fall in the case of secondary amines and rise in the case of tertiary amines, along the homologous series of the amine alcohols prepared.

All the amino alcohols prepared form well-crystallized picrolonates. Their melting points (given in the table) decrease regularly along the homologous series.

From the addition of ammonia and amines to isoprene α-oxide, one would expect the formation in each case of two isomeric amino alcohols with a primary and a tertiary hydroxy group.



(I) (II)

As Krasusskii's rule for reactions of primary-tertiary oxides in alkaline reagents is closely followed [2], we assigned structure (I) to the products of ammonia and amine addition to isoprene oxide.

With the purpose of finding other possible isomers of the amino alcohols, we carried out another experiment on the addition of methylamine to isoprene oxide, using considerably greater amounts of the starting materials. Distillation of the reaction products from this experiment gave, in addition to the amino alcohol described in the table, another amino alcohol (10-12% of the mixture) with a higher boiling point.

A comparison of the infrared spectra of these isomeric amino alcohols leaves no doubt that both contain a vinyl group. The double bond gives a band at 1646 cm^{-1} in both spectra and the bands at 923-926 cm^{-1} (strong) and 990-1003 cm^{-1} (average) correspond to the CH-deformation vibrations in the vinyl group. The two substances have equal absorptions at 6100 cm^{-1} which is very characteristic of vinyl compounds [3]. Consequently, the amino alcohol with the higher boiling point could only be assigned formula (II).*

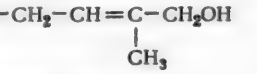
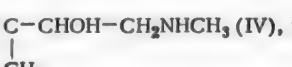
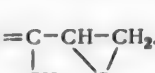
* Besides Formulas (I) and (II), the isomeric amine alcohols could have formula  (III) (1,4-addition) or formula  (IV), if the initial oxide contained traces of the isomer  . Both of these formulas are excluded.

TABLE 1

Constants and Data for the Obtaining of Amino Acids

Substance	Boiling point at 20 mm	d_4^{20}	n_D^{20}	MR_D		Found (%)			Calculated (%)			Picrolonates		
				found	calc.	C	H	N	C	H	N	melting point	% N	
													found	calc.
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2NH_2$	75—75.5°	0.9581	1.4698	29.44	29.77	59.44	10.90	—	59.37	10.96	—	195—196°	18.73	19.17
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2NHCH_3$	59.5—60	0.9040	1.4522	34.38	34.57	62.32, 62.44	11.67, 11.52	12.38, 12.30	62.56	11.38	12.16	214—215	18.38, 18.55	18.46
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2NHC_2H_5$	70—71	0.8821	1.4509	39.43	39.19	65.36, 65.42	11.78, 12.01	11.28, 11.19	65.07	11.70	10.84	195—196	17.53, 17.83	17.81
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2NHC_3H_7$	82—83	0.8726	1.4461	43.78	43.80	66.88, 67.03	12.06, 12.07	9.86, 9.89	67.08	11.96	9.78	188—189	16.97, 17.12	17.19
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2NHC_4H_9$	97—99	0.8670	1.4470	48.46	48.42	68.48, 68.62	12.29, 12.21	9.05, 9.15	68.74	12.17	8.91	179—180	16.49, 16.34	16.62
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2N(CH_3)_2$	50.5—51.5	0.8584	1.4378	39.49	39.53	65.23, 64.97	11.88, 11.92	11.01, 10.92	65.07	11.70	10.84	136—137	17.56, 17.66	17.81
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2N(C_2H_5)_2$	75—76	0.8513	1.4394	48.62	48.76	68.82, 69.19	12.06, 12.23	9.05, 9.31	68.74	12.17	8.91	119—120	16.80, 16.69	16.62
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2N(C_3H_7)_2$	100—102	0.8483	1.4421	57.81	58.00	71.68, 71.54	12.50, 12.64	7.37, 7.48	71.30	12.51	7.56	98—99	15.95, 15.69	15.58
$CH_2=CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}OH-CH_2N(C_4H_9)_2$	127—128	0.8470	1.4444	66.97	67.23	72.92, 73.10	12.89, 12.88	6.83, 6.73	73.18	12.75	6.57	94—95	14.67, 14.40	14.67

The same frequencies are found in the spectrum of the amino alcohol prepared from isoprene oxide and dimethylamine.

Thus,using methylamine as an example, it was shown that amines were added to isoprene oxide in two directions; however, a very small degree of addition, contrary to V. V. Markovnikov's rule, occurred.

EXPERIMENTAL

Isoprene oxide (1,2-epoxy-2-methylbutene-2) was prepared by distilling the bromohydrin over alkali and the former was obtained from isoprene by the method described previously [4]. About 150 g of oxide with b. p. 79-80°, d^{20}_4 0.8547, $n^{20}D$ 1.4142 was used for the work.

When isoprene oxide was reacted with a 10-fold excess of 33% aqueous ammonia solution under normal conditions, the yield of monoalkenolamine was about 50%. In addition we obtained a higher fraction, which partly crystallized. It was not examined more closely.

When isoprene oxide (0.1-0.2 mole) was reacted with 3-5-fold excess of 33% aqueous solutions or emulsions of amines (the mixture of reagents was stirred for several hours and then left to stand for 1-2 days), the yields of amino alcohols varied over the range 60-75%. Analytical data for all the compounds isolated are given in the table.*

A large-scale experiment using 48 g of isoprene oxide and 170 g of methylamine yielded 52 g of a mixture of amino alcohols, which was vacuum distilled to give the amino alcohol described in the table (44 g) and an amino alcohol with the constants given below (4.5 g).

B. p. 87-89° (20 mm), d^{20}_4 0.9356, $n^{20}D$ 1.4624. Found %: C 62.41; H 11.34; N 12.65. $C_6H_{13}ON$. Calculated %: C 62.57; H 11.38; N 12.16.

The picrolonate had m. p. 187-188°.

SUMMARY

1. The reaction of isoprene oxide with ammonia and some primary and secondary amines was investigated.

2. It was established that the reaction gave mainly unsaturated amino alcohols with a tertiary alcohol group. Using methylamine as an example, it was shown that isomeric amino alcohols with a primary alcohol group were obtained as 10-12% amounts of the mixture.

3. Ten unsaturated amino alcohols were prepared and characaterized. Crystalline picrolonates were prepared from all the substances.

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* The analyses were performed by I. A. Maretina, and the authors would like to thank her for them.

** Original Russian pagination. See C. B. translation.

*** In Russian.

INVESTIGATION OF ISOMERIZATION AND DIMERIZATION OF DIMETHYLVINYLCARBINOL RELATIVE TO THE pH OF THE REAGENT

III. THE EFFECT ON DIMETHYLVINYLCARBINOL OF HYDROCHLORIC ACID, SATURATED WITH SODIUM AND MAGNESIUM CHLORIDES, AND HYDROFLUORIC ACID

A. I. Lebedeva and L. F. Almashi

The investigation of dimethylvinylcarbinol reactions in relation to the pH of the reagent was begun in previous papers [1, 2]. In the present work we decided to try the effect on dimethyvinylcarbinol of such strongly acid reagents as hydrofluoric acid and saturated solutions of sodium and magnesium chlorides in hydrochloric acid at various concentrations.

The pH was measured potentiometrically with a hydrogen electrode.

Reaction of the above reagents with dimethylvinylcarbinol gave a mixture of products from which we isolated and identified isoprene, the original dimethylvinylcarbinol, γ,γ-dimethylallyl alcohol, the γ,γ-dimethylallyl ether of dimethylvinylcarbinol, the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, linalool and geraniol. Table 1 gives the yields of the products obtained as percents of the dimethylvinylcarbinol that reacted.

The results obtained show that with a decrease of the pH of the reagent, the amount of dimethylvinylcarbinol recovered from the reaction decreased and the yield of terpene alcohols increased.

A certain similarity may be drawn here with the data given by Komarewsky and Shih [3], who established that the polymerization of isoprene depended on the concentration of acids at room temperature. For some reason the authors did not note in their work that the yield of dimer and polymer fractions was very strongly affected by not only the concentration, but also the strength of the acid, as at equal concentrations, sulfuric acid has a much greater effect than phosphoric acid. It should be noted that with a decrease in the pH of the reagent, the yield of

TABLE 1

Expt. no.	Reagent	pH of Reagent	Isoprene	Dimethylvinylcarbinol recovered	γ,γ-Dimethylallyl alcohol	γ,γ-Dimethylallyl ether of		Linalool	Geraniol
						dimethylvinylcarbinol	γ,γ-dimethylallyl alcohol		
1	1-N HCl, saturated with NaCl	+0.15	6.0	34.0	12.1	9.0	2.4	Traces	Traces
2	1-N HCl, saturated with $MgCl_2$	—0.18	7.6	21.4	8.9	20.4	5.0	2.0	Traces
3	1-N HF	—0.25	10.0	20.4	7.5	22.6	8.0	3.0	Traces
4	5-N HF	—0.96	14.8	17.6	9.7	14.5	6.0	6.0	3.1
5	10-N HF	—1.43	9.0	12.0	4.5	9.0	17.0	9.0	4.5
6	10-N HCl, saturated with NaCl	—1.76	10.8	6.4	3.8	8.7	16.6	8.9	3.2
7	10-N HCl, saturated with $MgCl_2$	—1.93	12.7	6.3	2.3	10.5	14.8	10.5	4.2

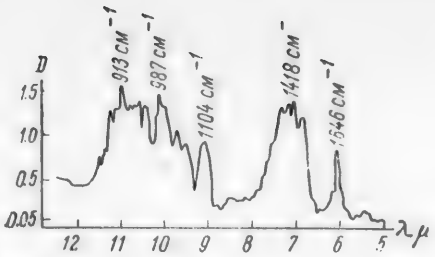

Fig. 1. Infrared spectrum of dimethylvinylcarbinol.

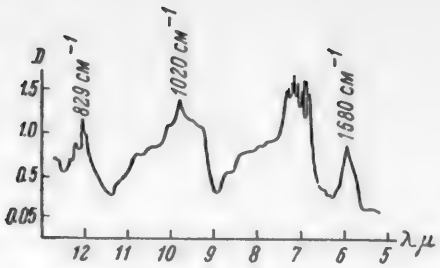

Fig. 2. Infrared spectrum of β,β-dimethylallyl alcohol.

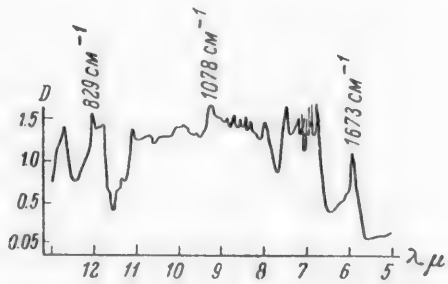

Fig. 3. Infrared spectrum of γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol.

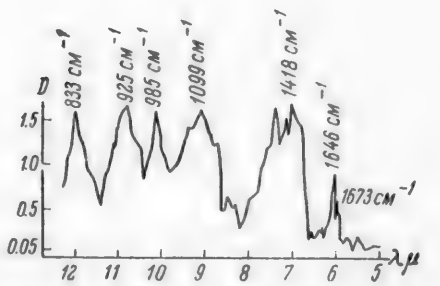

Fig. 4. Infrared spectrum of linalool (synthetic).

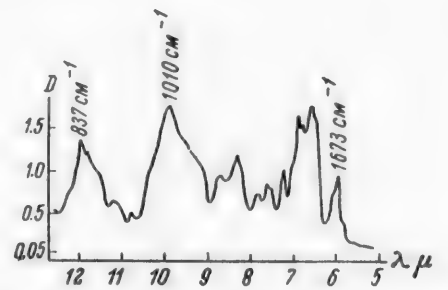

Fig. 5. Infrared spectrum of geraniol (synthetic).

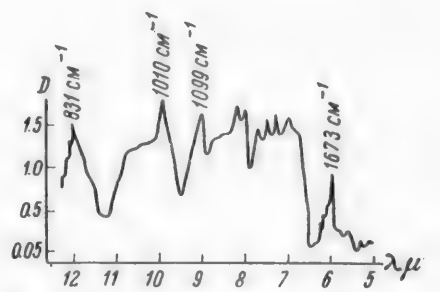

Fig. 6. Infrared spectrum of geraniol hydrate.

isoprene and unsaturated ethers increased and this indicated a considerable and, in this case, unwanted acceleration of the processes of molecular and intermolecular dehydration. Another interesting fact is that with a decrease in pH the yield of primary-tertiary ether decreased and the yield of diprimary ether increased, but the total yield of unsaturated ethers remained almost constant.

In addition to linalool and geraniol, Expts. 6 and 7 yielded a higher boiling fraction (2 and 4%, respectively) which according to elementary analysis, active hydrogen content, molecular weight determination and physical constants could be considered geraniol hydrate, first prepared by Pfauu and Plattner [4].

Most probably, the geraniol hydrate was formed in this case by geraniol hydration.

Raman (Table 3) and IR spectra were plotted for the compounds isolated (Figs. 1-6). The most characteristic data are given in Table 2.

The data obtained show that the Raman spectra of dimethylvinylcarbinol and linalool have maxima with frequencies of 1642-1643 cm^{-1}, which indicate a primary-tertiary double bond [5]. The presence of this bond is confirmed in the IR spectra by the frequencies 1646 and 1418 cm^{-1}. The Raman spectra of γ,γ-dimethylallyl

TABLE 2

Compound	$\Delta\nu$ cm^{-1} in the Raman spectrum	ν in the IR spectrum
Dimethylvinylcarbinol	1643 (10)	1646, 1418, 1104, 987, 913
γ,γ-Dimethylallyl alcohol	1676 (10)	1680, 1020, 829
γ,γ-Dimethylallyl ether of γ,γ-dimethylallyl alcohol	1674 (10)	1673, 1078, 829
Linalool	1674 (10), 1642 (8)	1673, 1646, 1418, 1099, 985, 925, 853
Geraniol	1674 (10)	1673, 1010, 837
Geraniol hydrate	—	1673, 1099, 1010, 831

TABLE 3

Compound	Boiling point (pressure in mm)	ν cm^{-1} in Raman spectra
Dimethylvinylcarbinol	96—97°	3086 (1); 3046 (4); 3008 (1); 2976 (5); 2921 (4); 2867 (2); **1643** (10); 1449 (6); 1407 (2); 1289 (6); 1231 (1); 1031 (1); 946 (5); 917 (4); 885 (2); 726 (10); 670 (0.5)
γ,γ-Dimethylallyl alcohol	49 (10)	2978 (2); 2918 (4); 2864 (2); **1676** (10); 1450 (8); 1379 (8); 1327 (2); 1297 (1); 1241 (1); 1181 (2); 1108 (2); 1068 (1); 1003 (1); 933 (1); 881 (1); 774 (4); 729 (1); 511 (1); 368 (1); 239 (1)
γ,γ-Dimethylallyl ether of γ,γ-dimethylallyl alcohol	55 (3)	2973 (1); 2919 (2); **1674** (10); 1446 (7); 1379 (5); 1327 (3); 1241 (1); 1196 (0.5); 1121 (1); 1056 (1); 1007 (2); 933 (0.5); 765 (1)
Linalool	69 (3)	3128 (3); 3047 (2); 2980 (5); 2920 (8); 2464 (5); **1674** (10); **1642** (8); 1448 (10); 1412 (1.5); 1379 (5); 1306 (2); 1229 (2); 1142 (2); 1076 (3); 1027 (1); 922 (1); 839 (1); 818 (1); 759 (2); 720 (1); 628 (1); 542 (1); 256 (2)
Geraniol	98 (3)	3041 (1); 2971 (2); 2919 (4); 2854 (2); **1674** (10); 1446 (8); 1378 (4); 1320 (1); 1077 (0.5); 1041 (0.5); 910 (0.5); 794 (0.5); 721 (1); 249 (0.5)

alcohol, γ,γ-dimethylallyl ether, linalool, geraniol and geraniol hydrate contain the frequency 1674-1676 cm^{-1}, characteristic of a secondary-tertiary double bond. The IR spectra have characteristic maxima at 1673-1680 cm^{-1}, which correspond to the C=C bond vibration of a trisubstituted ethylene bond [6] and at 829-837 cm^{-1}, which correspond to the deformation vibration of C—H at the same bond. The frequency 1078 cm^{-1}, obtained in the case of γ,γ-dimethylallyl ether, may correspond to the C—O bond vibration of ethers. The frequency 1010-1020 cm^{-1} corresponds to the vibration of the C—O bond in primary alcohols.

The IR spectral data obtained for synthetic linalool and geraniol agree within the limits of experimental error with those in the literature [6].

EXPERIMENTAL

The reagent was added dropwise to 50 g of anhydrous dimethylvinylcarbinol, placed in a three-necked flask with a reflux condenser and a stirrer. The total amount of hydrochloric and hydrofluoric acids for each experiment was kept the same. For example, in Expt. 1 we used 50 g of 1 N HCl, saturated with NaCl, in Expt. 6, 5 g of 10 N HCl, saturated with NaCl, in Expt. 3, 50 g of 1 N HF and in Expt. 5, 5 g of 10 N HF. The mixture was stirred vigorously for 96 hrs at room temperature, 3 hrs at 30-40° and 3 hrs at 70-80°. The layers were then separated. The upper layer was washed with aqueous soda solution and dried with potassium carbonate. An ether extraction of the lower layer yielded original dimethylvinylcarbinol and traces of high boiling compounds. The upper layer was first roughly separated into three fractions and then each fraction was fractionated on a column.

The 1st fraction with b. p. 34-36° was mainly isoprene. The anhydride of 5-methyltetrahydrophthalic acid had m. p. 64°. The 2nd fraction corresponded to the original dimethylvinylcarbinol in its constants. The Raman spectrum was plotted with a 7-hr exposure and a 0.07 mm slit (Table 3). The infrared absorption spectrum was plotted on a Hilger spectrometer with a slit width of 1.2-2 cm^{-1}. The thickness of the absorbing layer was 45 μ (Fig. 1). The 3rd fraction consisted of γ,γ-dimethylallyl alcohol. The melting point of the acid 3-nitrophthalic ester was 128-129°, which corresponds to literature data [7]. The 4th fraction corresponded to the γ,γ-dimethylallyl ether of dimethylvinylcarbinol [2]. The 5th fraction was the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, the 6th linalool and the 7th geraniol. The geraniol was purified via its calcium chloride compound. The data are given in Fig. 5 and Tables 2 and 3.

Investigation of 8th fraction with b. p. 148-150° (10 mm).

$n^{19}D$ 1.4738, d^{19}_4 0.9484, MR_D 51.02; calculated 50.96. Found %: C 69.49; H 11.84; M 175.8; number of active hydrogens 1.96. $C_{10}H_{20}O_2$. Calculated %: C 69.72; H 11.70. M 172.3; number of active hydrogens 2.00.

2.8 g of the substance with b. p. 148-150° (10 mm) in 20 ml of chloroform was ozonized at −70°. 0.91 g of ozone was added. The ozonide (3.5 g) was decomposed with water. Traces of formaldehyde and formic acid were found. 66% of the theoretical amount of acetone was found. The IR spectrum of geraniol hydrate is given in Fig. 6 and Table 2.

SUMMARY

1. The effect of strongly acid reagents on dimethylvinylcarbinol was investigated and a definite relation of reaction product yields to pH of the reagent was found.

2. A decrease in the value of the reagents pH decreased the percent of dimethylvinylcarbinol recovered from the reaction and increased the yield of terpene fractions, i. e., a decrease in the pH of the reagent promoted dimerization and polymerization.

3. Strongly acid reagents reacted with dimethylvinylcarbinol to give, in addition to terpene alcohols, the product of their hydration — geraniol hydrate.

4. Raman spectra were plotted for dimethylvinylcarbinol, γ,γ-dimethylallyl alcohol, the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, synthetic linalool and geraniol.

5. IR spectra were plotted for dimethylvinylcarbinol, γ,γ-dimethylallyl alcohol, the γ,γ-dimethylallyl ether of γ,γ-dimethylallyl alcohol, synthetic linalool, geraniol and geraniol hydrate.

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INVESTIGATION OF ETHERS WITH A DOUBLE BOND IN THE ALLYL POSITION

III. STUDY OF THE ETHERIFICATION OF α,α,γ,γ-TETRAALKYL SUBSTITUTED ALLYL ALCOHOLS

V. I. Pansevich-Kolïada and I. F. Osipenko

In previous reports [1, 2] we showed that α,α,γ,γ-tetraalkyl substituted allyl alcohols very readily form ethers when treated with primary monoatomic alcohols of the aliphatic series in the presence of a small amount of sulfuric acid.

The present work is devoted to a study of how the etherification of tetraalkyl substituted allyl alcohols is affected by the structure of primary alcohols, the nature of the alcohol groups (primary, secondary, tertiary), the possibility of using heterofunctional compounds containing a primary alcohol group, for the etherification, and also the possibility of forming ethers of the allyl alcohols being studied with di- and triatomic alcohols.

With this in mind and using the conditions described previously [1, 2], we etherified 2,4-dimethylpenten-2-ol-4 (I), 2,4-dimethylhexen-2-ol-4 (II), 2,4-dimethylhepten-2-ol-4 (III) and 2,4-dimethylocten-2-ol-4 (IV) with various hydroxyl-containing compounds.

The reaction of alcohols (I and II) with allyl alcohols in the presence of sulfuric acid readily gave the corresponding diallyl ethers – 2,4-dimethyl-4-allyloxypentene-2 (V) and 2,4-dimethyl-4-allyloxyhexene-2 (VI).

Alcohol (IV) was readily etherified with benzyl alcohol and alcohol (II) with β-phenylethyl alchol to give 2,4-dimethyl-4-benzyloxyoctene-2 (VII) and 2,4-dimethyl-4-(β-phenylethoxy)-hexene-2 (VIII), respectively.

Etherification of alcohol (II) with heterofunctional compounds, ethylene chlorohydrin and β-ethoxyethanol, also gave ethers – 2,4-dimethyl-4-(β-chloroethoxy)-hexene-2 (IX) and 2,4-dimethyl-4-(β-ethoxyethoxy)-hexene-2 (X), respectively.

We studied the effect of the nature of the alcohol group of the second component on the etherification of α,α,γ,γ-tetraalkyl substituted allyl alcohols using the reaction of alcohol (II) with the secondary alcohols, propanol-2 and octanol-2. No ethers were formed in either case. No ethers were obtained from these alcohols and the tertiary alcohol 2-methylbutanol-2 and phenol. Under the same conditions, alcohol (III) and cyclohexanol gave a small yield of 2,4-dimethyl-4-cyclohexoxyheptene-2 (XI).

Thus, α,α,γ,γ-tetraalkyl substituted allyl alcohols were readily etherified only with those compounds which contain a primary alcohol group.

Allyl ethers of polyhydroxy compounds have been described several times in the literature [3-10]. Some of them have the valuable capacity of forming stable, transparent and insoluble films [3, 4]. It was therefore interesting to study the etherification of α,α,γ,γ-tetraalkyl substituted allyl alcohols with di- and triatomic alcohols.

We etherified alcohols (II), (III) and (IV) with ethylene glycol and glycerol. In the case of the ethylene glycol, the reaction proceeded analogously to the etherification with primary monoatomic alcohols and gave simultaneously the corresponding mono- and diethers of ethylene glycol (XII-XVI).

The reaction products of alcohols (II)-(IV) and glycerol were glycerol diethers. As α,α,γ,γ-tetraalkyl substituted allyl alcohols did not form ethers with secondary alcohols and as there were no glycerol triethers in the reaction products, the structure of the glycerol diethers we prepared could be expressed by the formulas (XVII)-(XIX).

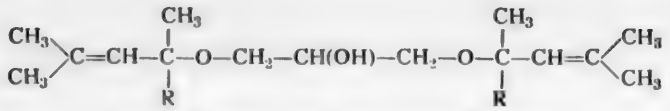
Characteristics of Ethers Obtained

Name of ether	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
2,4-Dimethyl-4-allyloxypentene-2 (V) $C_{10}H_{18}O$	49.5—50.5° (10)	1.4406	0.8240
2,4-Dimethyl-4-alloxyhexene-2 (VI) $C_{11}H_{20}O$	59.5—60.5 (9)	1.4431	0.8311
2,4-Dimethyl-4-(benzyloxy)-octene-2 (VII) $C_{17}H_{26}O$	132—133.5 (5—6)	1.4967	0.9174
2,4-Dimethyl-4-(β-phenylethoxy)-hexene-2 (VIII) $C_{16}H_{24}O$	132—132.5 (6)	1.4964	0.9205
2,4-Dimethyl-4-(β-chloroethoxy)-hexene-2 (IX) $C_{10}H_{19}OCl$	62—62.5 (2)	1.4522	0.9445
2,4-Dimethyl-4-(β-ethoxyethoxy)-hexene-2 (X) $C_{12}H_{24}O_2$	95.5—96.5 (10)	1.4374	0.8661
2,4-Dimethyl-4-cyclohexoxyheptene-2 (XI) $C_{15}H_{28}O$	101 (8)	1.4582	0.8718
2,4-Dimethyl-4-(β-hydroxyethoxy)-hexene-2 (XII) $C_{10}H_{20}O_2$	68—69 (1)	1.4534	0.9220
2,4-Dimethyl-4-(β-hydroxyethoxy)-heptene-2 $C_{11}H_{22}O_2$ (XIII)	86.5—88 (1.5)	1.4549	0.9104
2,4-Dimethyl-4-(β-hydroxyethoxy)-octene-2 $C_{12}H_{24}O_2$ (XIV)	94.5—95 (2)	1.4550	0.9006
1,2-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-ethane $C_{18}H_{34}O_2$ (XV)	112—114 (1)	1.4551	0.8814
1,2-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-ethane (XVI) $C_{22}H_{42}O_2$	161—163 (1—2)	1.4582	0.8688
1,3-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-propanol-2 (XVII) $C_{19}H_{36}O_3$	136.5—138 (1.5)	1.4646	0.9117
1,3-Di-(1,3-dimethyl-1-n-propylbuten-2-oxy)-propanol-2 (XVIII) $C_{21}H_{40}O_3$	143—144 (1)	1.4640	0.9133
1,3-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-propanol-2 (XIX) $C_{23}H_{44}O_3$	158.5—160 (1)	1.4639	0.9067
2,4-Dimethyl-4-(2,3-dihydroxypropoxy)-heptene-2 $C_{12}H_{24}O_3$ (XX)	134—136 (1)	1.4661	0.9651

• The high molecular weight of ether (XX) is probably due to association of the molecules of

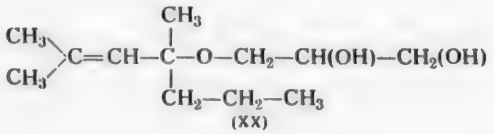
MR_D		Found (%)			Calculated (%)			M	
found	calc.	C	H	OH	C	H	OH	found	calc.
49.16	49.09	77.88	11.81	—	77.86	11.76	—	149.8, 153.0	154.24
53.65	53.70	78.34	12.36	—	78.50	12.27	—	163.9, 166.7	168.16
78.52	78.28	82.50	10.73	—	82.86	10.65	—	289.5, 242.4	246.2
73.80	73.66	82.69	10.66	—	82.70	10.41	—	—	—
54.49	54.42	—	—	—	—	—	—	187.7	190.7
60.64	60.53	72.10	12.20	—	71.95	12.08	—	189.5, 194.7	200.3
70.25	70.44	80.07	12.32	—	80.29	12.58	—	217.2, 217.5	224.2
50.54	51.08	69.66	11.72	10.00	69.72	11.70	9.87	173.2	172.26
55.52	55.70	70.90	12.14	9.49	70.92	11.91	9.12	—	—
60.35	60.38	72.20	12.35	8.12	71.95	12.08	8.49	196.3, 194.7	200.3
87.30	87.69	76.31	12.27	—	76.55	12.16	—	273.3	252.4
106.4	106.15	78.32	12.39	—	78.05	12.51	—	—	—
94.23	93.71	73.37	11.80	5.19	73.02	11.61	5.44	—	—
102.9	103.0	74.36	12.06	4.52	74.07	11.84	4.99	335.1	340.5
112.3	112.28	75.28	12.07	4.92	74.95	12.03	4.61	360.0, 354.4	368.6
62.02	61.84	67.01	11.15	15.45	66.62	11.19	15.72	241.2*, 244.2	216.3

this substance, which contains two OH groups.



(XVII) R = C_2H_5; (XVIII) R = n-C_3H_7; (XIX) R = n-C_4H_9

A glycerol monoether (XX) was also isolated in the case of alcohol (III).



(XX)

The effect of the size of the hydrocarbon radical of the primary monoatomic alcohol on the reaction rate was studied using as an example the etherification of alcohol (IV) with a mixture of equimolecular amounts of methyl and n-butyl alcohols. Under these conditions the ether yield for methyl alcohol was twice as great as for n-butyl. Consequently, the rate of etherification of alcohol (IV) with methyl alcohol was relatively higher than that with n-butyl.

EXPERIMENTAL

The tertiary alcohols (I-IV) were synthesized by the Grignard reaction from mesityl oxide and the appropriate alkylmagnesium halides [11, 12].

The ethers of $\alpha, \alpha, \gamma, \gamma$-tetraalkyl substituted allyl alcohols were prepared by the procedure described in the previous report [2], except that in the case of the glycerol ethers of alcohols (II-IV), stirring was replaced by shaking the reaction mixture for 4 hrs. All the ethers prepared were colorless liquids. They dissolved readily in organic solvents, but were insoluble in water and decolorized a 1% potassium permanganate solution. Their physical constants are given in the table.

2,4-Dimethyl-4-allyloxypentene-2 (V). To 275 g (2.41 moles) of 2,4-dimethylpenten-2-ol-4 (I) was added 250 g (4.3 moles) of allyl alcohol, containing 10 ml of sulfuric acid solution. We obtained 209 g (56.2%) of ether.

2,4-Dimethyl-4-allyloxyhexene-2 (VI) was prepared from 10 g of 2,4-dimethylhexen-2-ol-4 (II) (0.078 mole) and 9.8 g (0.169 mole) of allyl alcohol, containing 0.5 ml of sulfuric acid solution. The yield was 6.8 g (53.8%) of ether.

2,4-Dimethyl-4- (β-phenylethoxy)-hexene-2 (VIII). 10 g (0.082 mole) of β-phenylethyl alcohols, containing 0.2 ml of sulfuric acid solution was added to 5 g (0.039 mole) of 2,4-dimethylhexen-2-ol-4 (II). We obtained 4.53 g (44.8%) of ether as a colorless liquid with an almond smell.

2,4-Dimethyl-4-(β-chloroethoxy)-hexene-2 (IX). 14.2 g (0.175 mole) of 2-chloroethanol, containing 0.5 ml of sulfuric acid solution, was added to 10 g (0.078 mole) of alcohol (II). We obtained 7.34 g (49.3%) of ether as a colorless mobile liquid with a slightly irritating smell.

Found %: Cl 18.11. $C_{10}H_{19}OCl$. Calculated %: Cl 18.59.

2,4-Dimethyl-4-(β-ethoxyethoxy)-hexene-2 (X) was prepared from 10.2 g (0.079 mole) of alcohol (II) and 18.69 g (0.23 mole) of 2-ethoxyethanol, containing 1 ml of sulfuric acid solution. The yield of ether was 8.16 g (50.4%).

2,4-Dimethyl-4-(β-hydroxyethoxy)-hexene-2 (XII) was prepared from 10.2 g (0.079 mole) of alcohol (II) and 20.2 g (0.358 mole) of ethylene glycol, containing 1.2 ml of sulfuric acid solution. The product was an immobile, colorless liquid. The yield of the glycol monoether was 4.57 g (33.2%).

1,2-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-ethane (XV). 1.95 g (17.3%) of this substance was obtained at the same time as the glycol monoether (XII). It was a colorless, oily liquid.

1,3-Di-(1,3-dimethyl-1-ethylbuten-2-oxy)-propanol-2 (XVII). 30 g (0.326 mole) of glycerol, containing 2 ml of aqueous sulfuric acid solution, was added to 15 g (0.117 mole) of alcohol (II). We obtained 4.02 g (21.9%) of the diether of glycerol as a colorless, immobile liquid.

2,4-Dimethyl-4-cyclohexoxyheptene-2 (XI) was prepared from 10 g (0.07 mole) of 2,4-dimethylhepten-2-ol-4 (III) and 14 g (0.14 mole) of cyclohexanol, containing 1 ml of sulfuric acid solution. It was a clear, colorless liquid. The yield of ether was 0.57 g (3.6%).

2,4-Dimethyl-4-(β-hydroxyethoxy)-heptene-2 (XIII). 22.2 g (0.358 mole) of ethylene glycol, containing 1 ml of sulfuric acid solution, was added to 15 g (0.105 mole) of alcohol (III); a colorless immobile liquid was formed. The yield of ether was 6.9 g (55.5%).

2,4-Dimethyl-4-(2,3-dihydroxypropoxy)-heptene-2 (XX) was prepared from 15 g (0.105 mole) of alcohol (III) and 25.2 g (0.247 mole) of glycerol, containing 1 ml of aqueous sulfuric acid solution. We obtained a colorless, viscous liquid, which represented a 1.7 g (8.2%) yield of the monoether.

1,3-Di-(1,3-dimethyl-1-n-propylbuten-2-oxy)-propanol-2 (XVIII). This colorless, viscous substance was obtained at the same time as (XX) in 18.9% yield.

2,4-Dimethyl-4-(benzyloxy)-octene-2 (VII). 160 g (1.48 mole) of benzyl alcohol, containing 2.5 ml of sulfuric acid solution, was added to 120 g (0.755 mole) of 2,4-dimethylocten-2-ol-4 (IV). We obtained 120.8 g (63.4%) of the ether. The colorless, oily liquid had an ethereal smell, slightly reminiscent of the smell of benzyl alcohol.

2,4-Dimethyl-4-(β-hydroxyethoxy)-octene-2 (XIV) was obtained from 23.4 g (0.15 mole) of alcohol (IV), 18.6 g (0.3 mole) of ethylene glycol and 0.5 ml of sulfuric acid solution. The yield of the glycol monoether was 9.77 g (32%).

1,2-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-ethane (XVI). The colorless immobile liquid was obtained at the same time as the monoether (XIV) in 13% yield.

1,3-Di-(1,3-dimethyl-1-n-butylbuten-2-oxy)-propanol-2- (XIX) was obtained from 29.4 g (0.15 mole) of alcohol (IV), 27.6 g (0.3 mole) of glycerol and 1.5 ml of sulfuric acid solution. We obtained a colorless, immobile liquid (3.5 g, 12.7%), which was the ether.

Etherification of 2,4-dimethylocten-2-ol-4 (IV) with a mixture of methyl and n-butyl alcohols. 15.6 g (0.1 mole) of alcohol (IV) was placed in a round-bottomed flask, fitted with a mechanical stirrer and a thermometer. With vigorous stirring, a mixture of 3.2 g (0.1 mole) of methyl alcohol, 7.4 g (0.1 mole) of n-butyl alcohol and 1 ml of aqueous sulfuric acid (1 : 5) was added in one portion. After 2.5 min, the reaction mixture, which was originally homogeneous and clear, instantaneously became turbid and its temperature rose from 16.3 to 21.4°. Stirring was continued for 30 min. Then the reaction mixture was treated by the method described previously [2] and vacuum distilled. We obtained two ethers – 2,4-dimethyl-4-methoxyoctene-2 (6.75 g, 39.6%) with b. p. 72.5-75° (10 mm), $n^{20}D$ 1.4371, d^{20}_4 0.8231 and 2,4-dimethyl-4-n-butoxyoctene-2 (4.05 g, 19.07%) with b. p. 104-105° (10 mm), $n^{20}D$ 1.4396, d^{20}_4 0.8219. We described both of these ethers in a previous report [2].

SUMMARY

1. The etherification of α,α,γ,γ-tetraalkyl substituted allyl alcohols with alcohols of various structures was studied.

2. It was established that the etherification of α,α,γ,γ-tetraalkyl substituted allyl alcohols proceeds only with compounds containing a primary alcohol group.

3. The rate of the etherification depends on the size of the hydrocarbon radical in the primary alcohol.

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INVESTIGATION OF OXIDO COMPOUNDS

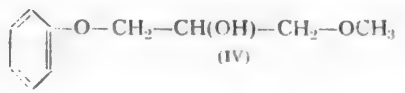
XI. REACTION OF α-OXIDES OF ALLYL ETHERS OF PHENOL, p-CRESOL AND GUAIACOL WITH METHYL ALCOHOL

V. I. Pansevich-Koliada and Z. B. Idel'chik

As is known, α-oxides react readily with alcohols and other oxide compounds in the presence of catalysts. This reaction was first applied by N. A. Prilezhaev [1] to 2-methylpropene-1 oxide and has since been studied many times using other α-oxides with various hydroxyl-containing compounds and catalysts [2-19]. The products of α-oxide reactions with alcohols are usually partial ethers of α-glycols. The structure of these ethers was determined by the order of opening of the oxide ring, which in its turn depended on the structure of the α-oxides and the nature of the catalyst used.

In the present work we studied the reaction of α-oxides of allyl ethers of phenol (I), p-cresol (II) and guaiacol (III) with methyl alcohol in the presence of sodium methylate.

The α-oxides (I, II, III) were reacted with methyl alcohol, in which metallic sodium was first dissolved, by heating in sealed glass ampoules in a tubular furnace. We established the presence of mixed partial ethers of glycerol in the reaction products. As was shown using a series of α-oxides, in the presence of catalysts of an alkaline character, the three-membered oxide ring opens at the bond of the oxide oxygen with the more hydrogenated carbon atom and, therefore, the glycerol ethers we obtained most probably have the following structures: 1-methoxy-3-phenoxy-propanol-2 (IV), 1-methoxy-3-(p-tolyloxy)-propanol-2 (V) and 1-methoxy-3-(o-methoxyphenoxy)-propanol-2 (VI). Such structures are more probable from the point of view of steric hindrance.



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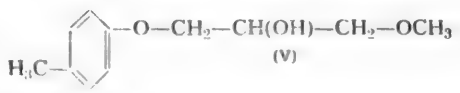

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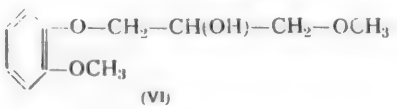

(VI)

EXPERIMENTAL

1. Preparation of 1-methoxy-3-phenoxypropanol-2 (IV). 5.5 g of the oxide of allyl phenyl ether (I) [20] was placed in a glass ampoule with 12 ml of methyl alcohol, in which 1 g of metallic sodium had been dissolved, A green ring formed at the boundary of the liquids and after shaking, the whole liquid acquired a brown color. After being heated in the sealed ampoule for 1.5 hrs on a water bath, the liquids had not mixed. After being heated at 100° for 6 hrs in a tubular furnace, the reacting mixture did not separate into layers. No pressure was found on opening the tube. The contents of the tube were poured into water. The yellowish oil which separated was extracted with ether, dried with $MgSO_4$ and vacuum distilled after removal of the ether. We obtained 3.4 g of a colorless, oily liquid with a sharp, tobacoo-like smell.

B. p. 134° (7 mm), $n^{20}D$ 1.5168, d^{20}_4 1.1130, MR_D 49.46; calculated 49.59. Found %: C 65.38; H 7.84; OH 8.28. M 183.4. $C_{10}H_{14}O_3$. Calculated %: C 65.93; H 7.69; OH 9.10. M 182.

2. Preparation of 1-methoxy-3-(p-tolyloxy)-propanol-2 (V). 2.7 g of the α-oxide of allyl p-cresyl ether (II) [21] and 5 ml of methanol, in which 0.25 g of metallic sodium had been dissolved, were heated in a glass ampoule in a tubular furnace for 3 hrs at 95°. The reaction products were treated as in the previous experiment. Distillation of the reaction products gave 0.6 g of a thick, colorless liquid with an ethereal smell.

B. p. 122° (2 mm), $n^{20}D$ 1.5135, d^{20}_4 1.0805, MR_D 54.37; calculated 54.21. Found %: C 67.96; H 8.86; OH 8.66. M 196.1. $C_{11}H_{16}O_3$. Calculated %: C 67.35; H 8.16; OH 8.67. M 196.0.

3. Preparation of 1-methoxy-3-(o-methoxyphenoxy)-propanol-2 (VI). 1.8 g of the α-oxide of the allyl ether of guaiacol (III) [21] and 3.5 ml of methanol, in which 0.25 g of metallic sodium had been dissolved, were heated in a glass ampoule in a tubular furnace for 5 hrs at 100°. The reaction products were then treated as in the previous experiments. Vacuum distillation of the reaction products yielded 0.5 g of a colorless, oily liquid, which had the smell of tobacco tar.

B. p. 155° (5 mm), $n^{20}D$ 1.5233, d^{20}_4 1.1439, MR_D 56.65; calculated 55.85. Found %: C 62.97; H 7.57; OH 7.52. M 220.8, 223.0. $C_{11}H_{16}O_4$. Calculated %: C 62.26; H 7.55; OH 8.00. M 212.0

SUMMARY

1. α-Oxides of allyl ethers of phenol, p-cresol and guaiacol were reacted with methyl alcohol in the presence of sodium methylate.

2. Three mixed partial ethers of glycerol (1-methoxy-3-phenoxy-propanol-2, 1-methoxy-3-(p-tolyloxy)-propanol-2 and 1-methoxy-3-(o-methoxyphenoxy)-propanol-2) were prepared.

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THE ABNORMAL PRODUCTS OF VINYL-1-CYCLOHEXENE-3 OZONOLYSIS

A. I. Iakubchik, A. I. Spasskova, and B. I. Tikhomirov

It was noted long ago that ozonolysis products may contain materials whose formation could not be explained on the basis of the usual scheme of ozonide formation and decomposition. These materials were then called abnormal ozonolysis products. Further work and improved analysis methods showed that the formation of abnormal products in ozonolysis is a very widespread phenomenon [1, 2]. During the abnormal course of ozonization or decomposition of an ozonide, the following may occur:

1) The formation of two types of ozonides – monomer and polymer, with the formation of polymer ozonide considered as the abnormal reaction [3, 4].

2) The transfer of the double bond during ozonization [5].

3) The formation of ozonides of α-hydroperoxides, when the ozone is not only added to the double bond but also acts as a catalyst for oxidation by oxygen [2, 6].

4) The oxidizing effect of ozone [7].

5) A formate-peroxide rearrangement; Ziegler [2] found some experimental justification for this. The class of materials in which a tertiary carbon atom is in a position α to the double bond, are extremely susceptible to extraneous effects. Ziegler explained this by the lability of the bond between the tertiary carbon atom and the carbon atom at the double bond [8].

6) A change in the aldehyde intermediate reaction products. Ziegler established that on treating α-amylcaproaldehyde with acetyl hydroperoxide only 28% of α-amylcaproic acid and 48% of volatile neutral materials were obtained [2].

7) The decomposition of acids, formed by oxidative decomposition of ozonides when treated with oxidants, for example, acetyl hydroperoxide [9]. There are indications that levulinic acid undergoes changes under the effect of oxidants and light [10].

The problem of the character and extent of the course of an abnormal reaction cannot be solved simply even for substances with well-known structures. In the case of high polymers, in particular caoutchoucs, the problem is much more complicated. Some information on the possible directions of abnormal reactions may be obtained by studying the behavior of a model substance, whose structure is known and at the same time has structural characteristics similar to those of caoutchouc. Vinyl-1-cyclohexene-3 may act as a model for divinyl caoutchouc. The former is composed of two divinyl molecules, connected in positions 1,2 and 1,4. The double bond in the ring corresponds to the inner double bond and the ethylene of the vinyl group to the outer double bond of the divinyl caoutchouc macromolecules.* Other characteristics in common are a methylene group in a position α to the double bond and a labile bond between the tertiary carbon atom and the carbon atom at the double bond.

Marvel [11] found 1,2,3-propanetricarboxylic acid in the products of oxidative decomposition of vinyl-1-cyclohexene-3 ozonide with hydrogen peroxide. He explained the formation of this acid by oxidative ozonolysis

* The double bond in the unit $-CH_2-CH=CH-CH_2-$ is called an inner and the double bond in the unit $-CH_2-\underset{\displaystyle CH=CH_2}{\underset{|}{CH}}-$ an outer bond.

of the α-methylene group. Ziegler [2] decomposed this ozonide with acetyl hydroperoxide. He found levulinic and succinic acids among the decomposition products. He explained their formation by a formate-peroxide rearrangement. On oxidizing vinyl-1-cyclohexene-3 with potassium permanganate, he found no levulinic acid, but an amount of succinic acid which was high in comparison with that obtained in the oxidative decomposition of the ozonide with acetyl hydroperoxide.

The purpose of our work was to study the products of oxidative decomposition of vinyl-1-cyclohexene-3 ozonide with acetyl hydroperoxide under the conditions used in our laboratory for the ozonolysis of divinyl caoutchoucs and to examine the effect of the α-methylene group and tertiary carbon atom, connected to the vinyl group, on the formation of abnormal ozonolysis products. The acids obtained by ozonide decomposition were separated by partition chromatography.

EXPERIMENTAL

The thermopolymerization was carried out with divinyl, regenerated with zinc in an aqueous alcohol solution from divinyl tetrabromide with m. p. 116-117°. The dimer formed in the polymerization was distilled on a column of 30 theoretical plates efficiency to yield vinyl-1-cyclohexene-3.

B. p. 66.5° (100 mm), d^{20}_4 0.8310, $n^{20}D$ 1.4642, MR 36.14; calculated 36.01.

The Raman spectrum was plotted on an ISP-51 spectrograph with a 0.07 mm slit and a 6-hr exposure:

236 (1), 277 (3), 316 (1), 354 (1), 379 (2), 413 (2), 481 (1), 512 (1), 665 (2), 727 (1), 805 (3), 869 (4), 920 (3), 964 (2), 1040 (1), 1078 (2), 1140 (1), 1191 (2), 1222 (1), 1251 (3), 1292 (6), 1332 (1), 1432 (7), 1641 (9), 1650 (10), 2837 (3), 2877 (2), 2918 (8), 2997 (3), 3023 (4), 3080 (2).

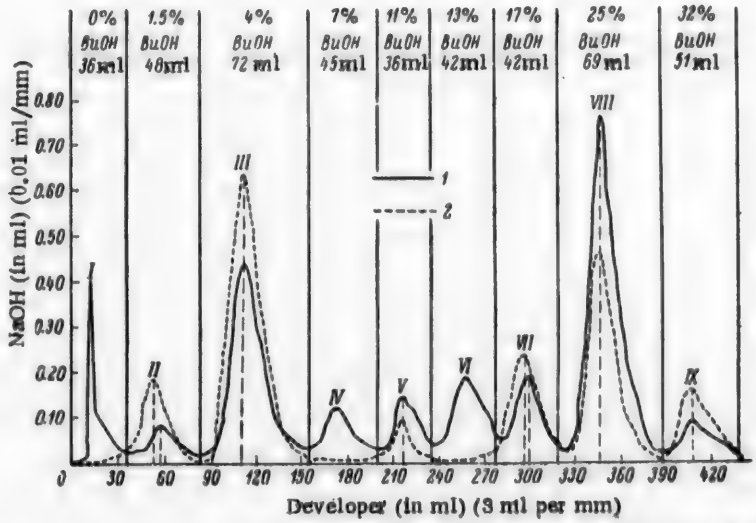

Fig. 1. Chromatograms. 1) Products of vinyl-1-cyclohexene-3 ozonolysis, 2) mixture of acids for identification of products of vinyl-1-cyclohexene-3 ozonolysis. The significance of the peaks is given in the text.

The line intensities given in brackets were evaluated visually relative to a scale of ten. The characteristics listed agree well with the data of other authors [11-14].

10 g of vinyl-1-cyclohexene-3 in ethyl acetate (b. p. 77-77.5°) was ozonized at −50°. Oxygen with a 5-6% ozone content was used for the ozonization. At the end of the ozonization, the solvent was distilled off at 15 mm and 20° until the ozonide had constant weight. Oxidative decomposition of the ozonide was performed with acetyl hydroperoxide in glacial acetic acid. Sufficient acetyl hydroperoxide was added to the ozonide solution to give 1 atom of active oxygen for each double bond. After 3 days, a two-fold amount of hydroperoxide was added and the solution was then left for a long time at room temperature. The excess hydroperoxide was decomposed with platinum black, prepared by Willstatter's method [15]. The acetic acid was distilled off at 1 mm and 30°. The products obtained formed a light yellow, viscous mass. For chromatographic analysis of the products of oxidative decomposition of vinyl-1-cyclohexene-3 ozonide, a column of 15 mm diameter was loaded with 13 g of MSK [3] grade silica gel, ground up with 9 ml of water. The height of the silica gel in the column was 140 mm. Water was the stationary solvent and water-saturated butanol−chloroform mixture the mobile one. The mobile solvent was passed through the column at 1 ml a minute. The solvent coming out of the column containing the acids was collected in 3 ml portions and titrated against 0.014 N sodium hydroxide in methyl alcohol. An alcohol solution of phenolphthalein was used as the indicator. The products of oxidative decomposition were put onto the column as a tertiary amyl alcohol (b. p. 100-100.5°) solution.

Peak Volume of Acids Investigated and Artificial Mixture, Made Up for Characterizing the Products Studied

Mixture separated	Peak volume (in ml):					
	Peak II − propionic acid	Peak III − acetic acid	Peak V − formic acid	Peak VII − succinic acid	Peak VIII − 1,2,4-butanetricarboxylic acid	Peak IX − 1,2,3-propanetricarboxylic acid
Artificial	54	114	216	297	348	408
Investigated	57	114	216	300	348	408

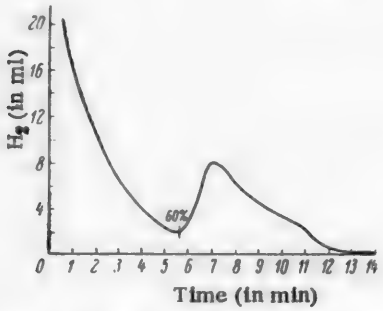

Fig. 2. Hydrogenation curve of vinyl-1-cyclohexene-3 with a Pd on $CaCo_3$ catalyst.

Figure 1 shows chromatograms of the mixture investigated and a mixture of propionic, acetic, succinic, 1,2,4-butanetricarboxylic and 1,2,3-propanetricarboxylic acids.

The table lists the peak volumes of the acids [16, 17] contained in the mixtures given above.

From Fig. 1 and the data in the table it follows that on the chromatogram of the mixture investigated, peak II corresponds to propionic, III to acetic, V to formic, VII to succinic, VIII to 1,2,4-butanetricarboxylic and IX to 1,2,3-propanetricarboxylic acids. The 1,2,4-butanetricarboxylic acid contained 3% of the carbon skeleton of vinyl-1-cyclohexene-3. Levulinic acid was not found among the decomposition products of the ozonide and a qualitative reaction for it [18] gave a negative result. It is possible that succinic acid arose from levulinic and 1,2,3-propanetricarboxylic from butanetricarboxylic acids. The presence of propionic acid indicated extensive decomposition of vinyl-1-cyclohexene-3 during the ozonolysis. There was no evidence as to the nature of peaks IV and VI. Peak I evidently consisted of a mixture of acids, which dissolved readily even in pure chloroform. It was shown chromatographically that the acetic acid, distilled off from the decomposition products of the ozonide, did not contain traces of other acids.

Since our problem also includes the consideration of whether the presence of a tertiary carbon atom connected to a carbon at the double bond, in the molecule, affects the abnormal reactions caused by the α-methylene group, we examined the behavior of ethyl-1-cyclohexene-3 during ozonolysis. Ethyl-1-cyclohexene-3 was prepared by selective hydrogenation of vinyl-1-cyclohexene-3 over a Pd on $CaCO_3$ catalyst. From the work of S. V. Lebedev and his co-workers [12, 19, 20], we expected that the vinyl group double bond would be hydrogenated much more rapidly than the double bond in the ring. The hydrogenation was carried out in a Lebedev apparatus and hydrogenation curves plotted by his method also [20]. A 0.30-0.35 g sample of vinyl-1-cyclohexene-3 was hydrogenated in ethyl alcohol in the presence of 0.1 g of catalyst. A hydrogenation curve obtained in one of these experiments is shown in Fig. 2.

By hydrogenating two samples of the substance on one catalyst, we found that the fall in the rate of hydrogenation, corresponding to the second arm of the curve, was due to a difference in the character of the bonds hydrogenated and not to exhaustion of the catalyst. In accordance with the above, vinyl-1-cyclohexene-3 was 60% hydrogenated. This should have given 80% of ethyl-1-cyclohexene-3 and 20% of ethylcyclohexane. Since for our purposes it was important that vinyl-1-cyclohexene-3 should be absent from the hydrogenation products but a trace of ethylcyclohexane would not interfere, it was decided to carry out the ozonization of ethyl-1-cyclohexene-3 in the presence of ethylcyclohexane. The hydrogenation products were treated with a saturated solution of calcium chloride several times to extract alcohol, dried over fused calcium chloride and sodium wire and distilled through a Vigreaux fractionating column, 15 cm high, at 69° and 100 mm pressure in an atmosphere of nitrogen. The product obtained had $n^{20}D$ 1.4463. According to the data in [12], the product of adding 50% hydrogen to vinyl-1-cyclohexene-3 has $n^{20}D$ 1.44847 and ethylcyclohexane $n^{20}D$ 1.43190. Ozonization, decomposition of the ozonide and separation of the ozonolysis products were performed under the conditions described above.

If the α-methylene group of the ethyl-1-cyclohexene-3 participated in the abnormal reactions, we would find β-ethylglutaric acid in the ozonolysis products. We synthesized this by Komnenos' method [21] for the chromatographic demonstration. β-Ethylglutaric acid was found in the ozonolysis products, which did not contain succinic, 1,2,4-butanetricarboxylic, 1,2,3-propanetricarboxylic and propionic acids, which must, therefore, only arise from substances containing labile 1,2 groupings.

SUMMARY

1. In addition to the normal products of vinyl-1-cyclohexene-3 ozonolysis (1,2,4-butanetricarboxylic and formic acids), abnormal products were found: succinic, 1,2,3-propanetricarboxylic and propionic acids.

2. An abnormal product, β-ethylglutaric acid, was found among the ozonolysis products of ethyl-1-cyclohexene-3.

3. The abnormal products are caused by the presence both of an α-methylene group and of a labile bond between the tertiary carbon atom and a carbon atom at the double bond.

4. In the ozonolysis products of divinyl caoutchoucs, whose macromolecules have the structural units 1,4, 1,2, 1,4, one would expect to find a low yield of 1,2,4-butanetricarboxylic and a high yield of succinic and 1,2,3-propanetricarboxylic acids.

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SYNTHESIS OF ACETIC ESTER OF BIS(HYDROXYCYCLOHEXYL)-1,3-BUTADIYNE AND ITS CATALYTIC HYDROGENATION

A. I. Nogaideli and G. M. Gonadze

In a previous paper [1] we described the synthesis of the acetic ester of 2,7-dimethyl-3,5-octadiyne-2,7-diol. In the hydrogenation of this ester it was established that in the presence of platinum black or colloidal palladium the addition of 8 atoms of hydrogen yields the acetate of the saturated alcohol and the diacetate of the saturated glycol, in which connection the diacetylenic ester is capable of adding a total of 5 moles of hydrogen to yield only the acetate of the saturated alcohol.

In this paper we decide to synthesize by the same method, but at a lower temperature, the acetic ester of bis(hydroxycyclohexyl)-1,3-butadiyne and study its catalytic hydrogenation. The latter was run in the presence of either colloidal palladium or platinum black. If when the hydrogenation is run in the presence of colloidal palladium the reaction is stopped after the addition of 8 atoms of hydrogen, then after suitable treatment of the hydrogenation product a clear mobile liquid of aromatic odor is obtained, the fractionation of which gave three substances: (I) – 1,4-dicyclohexylbutane, (II) – acetate of 1-hydroxycyclohexyl-4-cyclohexylbutane, and (III) – diacetate of 1,4-bis(1-hydroxycyclohexyl)butane. Small amounts of the starting diacetylenic ester and acetic acid were also isolated.

In the presence of platinum black the diacetylenic ester is capable of adding a total of 12 atoms of hydrogen, with a gradual reduction in the reaction rate, to yield only the saturated hydrocarbon (I). In the presence of colloidal palladium the diacetylenic ester absorbs about 75% of the theoretical amount of hydrogen in the first 10 min, while in the case of platinum black this phenomenon is not observed.

Consequently, it appears that a diacetylenic ester with cyclic radicals, in contrast to esters with aliphatic radicals, yields, in addition to the acetate of the saturated alcohol and the diacetate of the saturated glycol, the saturated hydrocarbon.

EXPERIMENTAL

Synthesis of bis(1-hydroxycyclohexyl)-1,3-butadiyne diacetate. A mixture of 20 g of the glycol with m. p. 173-174°, 100 g of acetic anhydride and 1 g of anhydrous sodium acetate was heated for 1 hr in an oil bath in a flask with reflux condenser at 165-170°; further treatment was the same as described before [1].

The yield of crystals with m. p. 86-87° (from alcohol) was 21 g (78%).

Found %: C 72.54, 72.60; H 8.42, 8.31; $2CH_3CO$ 26.11, 26.75. M 329, 333 (per Rast). $C_{20}H_{26}O_4$. Calculated %: C 72.72; H 7.88; $2CH_3CO$ 26.09. M 330.

The test for active hydrogen by the Chugaev-Tserevitinov method was negative. Saponification of the ester gave the original glycol.

Hydrogenation of bis(1-hydroxycyclohexyl)-1,3-butadiyne diacetate. For hydrogenation we took 3.30 g of the ester in 50 ml of ethyl alcohol. The colloidal palladium was prepared the same as before [1]. The hydrogenation results are given in the table.

After suitable treatment the product of hydrogenation over Pd was vacuum-distilled. Here the following substances were isolated: b. p. 126-128° (4-5 mm), 0.5 g (7.57%) (I); b. p. 148-150° (4-5 mm), 1.8 g (21.41%) (II) and b. p. 73-74°, 1.5 g (14.78%) (III).

Expt. nos.	Catalyst	Weight of catalyst (in mg)	Amount of hydrogen (in ml)		
			calc.	found	amount absorbed every 5 min
I	Colloidal Pd	5	1072 ($4H_2$)	1072	475, 325, 50, 25, 20, 15, 10, 10, 14.8, 12, 6; the remaining 102 ml required 2 hrs. A total of 1072 ml was absorbed in 3 hrs
2	Pt black	1000	1460 ($6H_2$)	1435	80, 60, 50, 35, 50, 40, 50, 35, 40, 45, 40; the remaining 893 ml required 3 hrs 10 min. A total of 1435 ml was absorbed in 4 hrs 10 min

Some of the original diacetylenic ester with m. p. 86-87° and some acetic acid was also isolated.

We ran a total of 3 parallel experiments, giving similar results.

After suitable treatment of the product of hydrogenation over Pt, we isolated 3 g of (I) with b. p. 126-128° (4-5 mm), and also 1.36 g of acetic acid, from the remaining liquid.

Here we ran a total of 2 parallel experiments, giving similar results.

Analysis of Substance (I) with B. p. 126-128° (4-5 mm)

d^{20}_4 0.8853, $n^{20}D$ 1.4840, MR_D 72.13; calculated 71.69. Found %: C 85.78, 87.27; H 13.29, 14.02. M 213, 218 (cryoscopic). $C_{15}H_{30}$. Calculated %: C 86.48; H 13.51. M 222.

The tests for both active hydrogen and triple bond were negative. The substance does not decolorize potassium permanganate solution.

Analysis of Substance with B. p. 148-150° (4-5 mm) (II)

d^{20}_4 0.9548, $n^{20}D$ 1.4750, MR_D 82.63; calculated 82.58. Found %: C 76.98; H 11.86; CH_3CO 15.35. M 275 (cryoscopic). $C_{18}H_{32}O_2$. Calculated %: C 77.14; H 11.42; CH_3CO 15.35. M 280.

Analysis of Substance with M. p. 73-74°

Found %: C 70.92, 71.15; H 10.88, 10.34; $2CH_3CO$ 25.68. M 325 (cryoscopic). $C_{20}H_{34}O_4$. Calculated %: C 71.00; H 10.06; $2CH_3CO$ 25.44. M 338.

SUMMARY

1. The acetic ester of bis(hydroxycyclohexyl)-1,3-butadiyne was synthesized and described for the first time, and its catalytic hydrogenation was studied.

It was shown that in the presence of colloidal palladium the addition of 8 atoms of hydrogen yields the hydrocarbon, the acetate of the saturated alcohol and the diacetate of the saturated glycol.

In the presence of platinum black the ester is capable of adding a total of 6 moles of hydrogen to yield the hydrocarbon.

2. The compounds 1,4-dicyclohexylbutane, 1-acetoxycyclohexyl-4-cyclohexylbutane and 1,4-bis(1-acetoxycyclohexyl)butane were isolated and described in this study.

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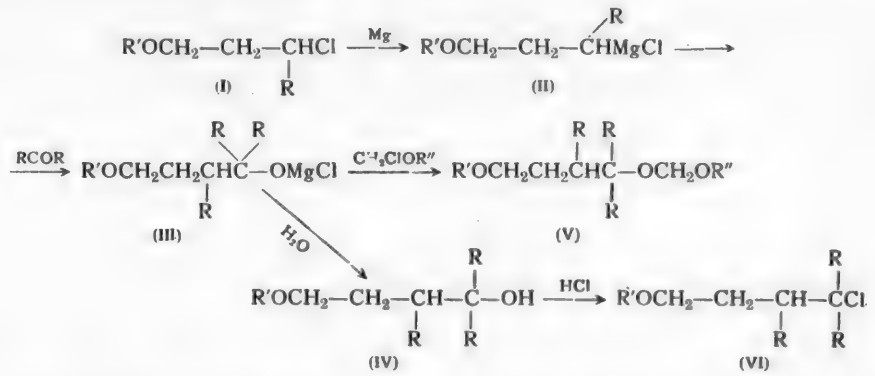
ETHERS OF GLYCOLS AND THEIR DERIVATIVES

XXXII. SYNTHESIS OF MONOETHERS OF γ-GLYCOLS AND THEIR ALKOXYMETHYL DERIVATIVES

Shamkhal Mamedov and A. F. Aliev

In a previous communication [1] we described the synthesis of a large number of γ-halo ethers (I), obtained by the alkylation of α-halo ethers with ethylenic hydrocarbons.

As a further aspect of studying the chemical transformations of γ-halo ethers (I), our purpose in the present study was to synthesize some 1,4-glycol monoethers (IV), some δ-alkoxy derivatives of the methylene glycol ethers (V), and some δ-chloro ethers (VI).



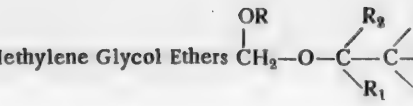
Organomagnesium compounds (II), prepared from γ-chloro ethers (I), react smoothly with aldehydes and ketones to yield magnesium chloroalkoxyalcoholates (III), which when treated with water yield 1,4-glycol monoethers (IV). However, in the experiments with acetophenone, together with compound (IV), a certain amount of methylphenylcarbinol and unsaturated ether is obtained, the formation of which can be explained on the basis on the basis of the free radical theory [2].

We synthesized the γ-chloro ethers (I) by the alkylation of α-chloro ethers with propylene and butylene [1]. As the carbonyl components we took acetaldehyde, benzaldehyde, acetone and acetophenone. In this manner we synthesized 17 new 1,4-glycol monoethers, the constants of which are given in Table 3.

By reacting various α-chloro ethers with magnesium chloroalkoxyalcoholates (III) by the method proposed by one of us [3], we synthesized 7 new δ-alkoxy derivatives of methylene glycol ether (ethers of δ-hydroxyacetals of formaldehyde) (see scheme), the constants of which are given in Table 1.

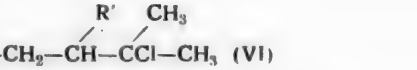
Reaction of the 1,4-diol monoethers (IV) with concentrated hydrochloric acid leads to replacement of the hydroxyl group on the tertiary carbon atom by chlorine with the formation of the corresponding δ-chloro ethers (VI). The reaction of replacing the hydroxyl by chlorine without the alkoxy group being attacked can to to completion only in the presence of a catalyst, a mixture of ammonium chloride and cuprous chloride. The constants of the obtained δ-chloro ethers are given in Table 2. An attempt to effect the reverse replacement of chlorine

TABLE 1

δ-Alkoxy Derivatives of Methylene Glycol Ethers  (V)

Expt. nos.	R	R_1	R_2	R_3	R_4	R_5	Name of monoether
1	CH_3	CH_3	CH_3	H	CH_3	C_4H_9-n	Formaldehyde methyl (α,α-dimethyl-β-methyl-δ-butoxy) butyl acetal
2	C_5H_{11}-iso	CH_3	CH_3	H	CH_3	C_4H_9-n	Formaldehyde isoamyl (α,α-dimethyl-β-methyl-δ-butoxy) butyl acetal
3	CH_3	CH_3	CH_3	H	C_2H_5	CH_3	Formaldehyde methyl (α,α-dimethyl-β-ethyl-δ-methoxy) butyl acetal
4	C_2H_5	CH_3	CH_3	H	C_2H_5	C_2H_5	Formaldehyde ethyl (α,α-dimethyl-β-ethyl-δ-ethoxy) butyl acetal
5	C_4H_9-n	CH_3	CH_3	CH_3	CH_3	C_2H_5	Formaldehyde butyl (α,α-dimethyl-β,β-dimethyl-δ-ethoxy) butyl acetal
6	C_4H_9-n	CH_3	CH_3	CH_3	CH_3	C_4H_9-n	Formaldehyde butyl (α,α-dimethyl-β,β-dimethyl-δ-butoxy) butyl acetal
7	C_2H_5	C_6H_5	H	H	CH_3	C_4H_9-n	Formaldehyde ethyl (α-phenyl-β-methyl-δ-butoxy) butyl acetal

TABLE 2

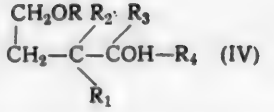
δ-Chloro Ethers  (VI)

Expt. nos.	Name of monoether	R	R′	Boiling point (pressure in mm)
1	1-Methoxy-4-methyl-3-ethyl-4-chloropentane	CH_3	C_2H_5	70—72° (11)
2	1-Ethoxy-4-methyl-3-ethyl-4-chloropentane	C_2H_3	C_2H_5	93—95 (10)
3	1-Butoxy-3,4-dimethyl-4-chloropentane	C_4H_9	CH_3	100—102 (6)
4	1-Isoamyloxy-3,4-dimethyl-4-chloropentane	C_5H_{11}	CH_3	102—103 (4)

Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		M		% C		% H		Yield (in %)
			found	calc.	found	calc.	found	calc.	found	calc.	
77.5—79° (10)	0.8984	1.4360	67.52	67.16	230.2	232	66.86	67.24	12.29	12.07	47.8
95—97 (9)	0.8453	1.4144	85.21	85.64	281.2	288	70.79	70.83	12.56	12.50	43.0
88—90 (24)	0.9236	1.4385	58.04	57.92	207.7	204	64.47	64.71	11.92	11.76	48.8
88—89 (15)	0.8670	1.4200	67.72	67.16	228.0	232	67.01	67.24	12.15	12.07	56.0
59—62 (4)	0.8475	1.4134	76.57	76.40	260.4	260	69.05	69.23	12.01	12.31	63.7
89—91 (3)	0.8550	1.4206	85.35	85.63	287.9	288	70.27	70.83	12.67	12.50	35.5
93—95 (36)	0.9916	1.4982	86.94	86.65	297.5	294	73.50	73.47	10.27	10.20	28.0

d_4^{20}	n_D^{20}	MR_D		M		Cl content (in %)		Yield (in %)
		found	calc.	found	calc.	found	calc.	
0.9435	1.4376	49.63	50.27	176.2	178.5	19.24	19.89	31.3
0.9214	1.4380	54.81	54.89	193.9	192.5	18.24	18.44	60.2
0.9120	1.4390	59.32	59.51	204.6	206.5	17.09	17.23	33.2
0.9047	1.4402	64.26	64.12	220.2	220.5	15.89	16.10	43.2

TABLE 3

1,4-Glycol Monoethers  (IV)

Expt. nos.	Name of monoether	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		M		% C		% H		% OH		Yield (in %)
					found	calc.	found	calc.	found	calc.	found	calc.	found	calc.	
1	1-Methoxy-3-methyl-4-pentanol	66—69° (4)	0.8917	1.4300	38.17	37.70	129.6	132	62.98	63.63	11.83	12.12	13.03	12.88	41.4
2	1-Ethoxy-3-methyl-4-pentanol	70—73 (3)	0.8947	1.4305	42.19	42.31	145.2	146	65.58	65.75	12.42	12.33	10.96	11.64	39.4
3	1-Butoxy-3-methyl-4-pentanol	90—91.5 (3)	0.8844	1.4330	51.00	51.55	174.2	174	68.72	68.96	12.63	12.65	10.23	9.77	33.5
4	1-Isoamyloxy-3-methyl-4-pentanol	87—89 (5)	0.8607	1.4210	55.39	56.10	186.4	188	70.04	70.21	12.80	12.76	9.50	9.04	31.6
5	1-Methoxy-3-ethyl-4-pentanol	76—78 (3)	0.9011	1.4310	41.94	42.31	144.2	146	65.70	65.75	12.36	12.33	12.10	11.64	44.67
6	1-Isoamyloxy-3-ethyl-4-pentanol	110—112 (5)	0.8592	1.4276	60.44	60.78	202.8	202	71.01	71.29	12.76	12.58	8.23	8.42	34.4
7	1-Methoxy-3,4-dimethyl-4-pentanol	66—67.5 (3)	0.9016	1.4360	42.34	42.31	147.9	146	65.79	65.75	12.06	12.33	11.90	11.64	36.06
8	1-Ethoxy-3,4-dimethyl-4-pentanol	76—78° (3)	0.8893	1.4436	47.75	46.93	163.3	160	67.27	67.50	12.46	12.50	10.47	10.62	34.3
9	1-Butoxy-3,4-dimethyl-4-pentanol	85—89 (3)	0.8897	1.4422	55.93	56.16	185.1	188	70.15	70.21	12.77	12.76	9.55	9.04	26.6
10	1-Isoamyloxy-3,4-dimethyl-4-pentanol	88—91 (3)	0.8730	1.4320	60.01	60.78	205.2	202	70.95	71.28	12.96	12.87	8.73	8.42	24.4
11	1-Butoxy-3-methyl-4-phenyl-4-butanol	83—85 (8)	0.9276	1.4748	71.60	71.74	235.2	236	76.14	76.27	10.14	10.17	7.42	7.20	57.5
12	1-Ethoxy-3-methyl-4-phenyl-4-pentanol	108—110 (18)	0.9643	1.4913	66.71	66.41	224.3	222	75.31	75.68	10.20	9.91	7.78	7.66	43.4
13	1-Butoxy-3,3-dimethyl-4-phenyl-4-pentanol	66—67 (3)	0.8890	1.4564	80.78	80.27	260.1	264	77.0	77.27	11.04	10.61	6.90	6.44	65.2
14	1-Methoxy-4-methyl-3-ethyl-4-pentanol	70—72 (3)	0.8999	1.4370	46.58	46.93	164.3	160	66.65	66.50	12.06	12.50	9.78	10.62	42.1
15	1-Butoxy-3,3,4-trimethyl-4-pentanol	102—103 (18)	0.8795	1.4392	60.43	60.78	198.4	202	71.21	71.29	12.36	12.87	9.15	8.42	32.6
16	1-Butoxy-3,3,4-trimethyl-4-pentanol	84—84.5 (2)	0.8702	1.4330	60.33	60.78	198.4	202	70.74	71.29	12.66	12.87	8.66	8.42	37.4
17	1-Isoamyloxy-4-methyl-3-ethyl-4-pentanol	80—83 (4)	0.8570	1.4300	65.11	65.40	213.0	216	72.11	72.22	12.92	12.96	7.50	7.87	30.7

by hydroxyl in the δ-chloro ethers proved unsuccessful. It was established that here even calcium carbonate cleaves HCl, leading to the formation of the unsaturated ether.

EXPERIMENTAL

Synthesis of 1-methoxy-3-methyl-4-pentanol (IV) (Table 1, compound 1). To the organomagnesium compound (II), prepared from 2.4 g of magnesium metal, 35 ml of ether and 13 g of methyl γ-chlorobutyl ether (I), was added 4.4 g of acetaldehyde with cooling. Then the stirring was continued for another 4 hrs at 40-45°. After standing for 8 hrs the complex was decomposed with slightly acid ice water. The reaction products were extracted from the lower layer with ether. The upper layer and the ether extract of the lower layer were combined, dried, the ether distilled off, and the residue vacuum-distilled twice.

Another 16 monoethers of type (IV) were synthesized in a similar manner (see Table 3).

Methyl (α,α,β-trimethyl-δ-butoxy)butyl ether of methylene glycol (V) (Table 1, compound 1) was obtained by reacting 8 g of methyl α-chloromethyl ether with the magnesium chloroalkoxyalcoholate (III) obtained from 16 g of butyl γ-chlorobutyl ether (I), 2.4 g of magnesium metal, 5.8 g of acetone and 40 ml of ether. The mixture was allowed to stand for 8 hrs, after which it was diluted with 50 ml of water. The upper layer was washed with 3% caustic solution, then with water, dried, and fractionally distilled in vacuo.

Six other new ethers of type (V) were synthesized in a similar manner (see Table 1).

δ-Chloro ethers (VI) were obtained in the following manner. To a mixture of 2.5 g of NH_4Cl, 1.25 g of Cu_2Cl_2 and 6 g of 1-methoxy-4-methyl-3-ethyl-4-pentanol (IV) was added 25 ml of concentrated hydrochloric acid (d 1.19) from a dropping funnel. After stirring for 2 hrs at room temperature the flask contents were diluted with an equal volume of water. The upper layer was washed with 3% caustic solution, then with water, and dried over Na_2SO_4. We isolated 2.4 g of 1-methoxy-4-methyl-3-ethyl-4-chloropentane (VI) (Table 2, compound 1).

Similar conditions were used to synthesize 3 other new δ-chloro ethers, the constants of which are given in Table 2.

SUMMARY

1. Seventeen new 1,4-diol monoethers of the aliphatic and aliphatic-aromatic series were synthesized and studied.

2. It was established that the organomagnesium method of synthesizing glycol ethers is suitable for the synthesis of the δ-alkoxy derivatives of methylene glycol ethers.

3. Seven new alkoxy derivatives of methylene glycol ethers were synthesized.

4. The hydroxyl group found at the tertiary carbon atom in 1,4-diol monoethers is easily replaced by chlorine when treated with concentrated hydrochloric acid in the presence of a catalyst ($NH_4Cl + Cu_2Cl_2$), leading to the formation of δ-chloro ethers.

5. Four new δ-chloro ethers were synthesized and studied.

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DIAMINES OF BENZIMIDAZOLE SERIES

I. SYNTHESIS AND PHYSICOCHEMICAL PROPERTIES OF DIAMINES

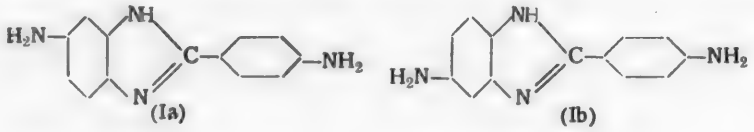
B. A. Porai-Koshits and Ch. Frankovskii

In this paper our purpose was to synthesize some diamines of the benzimidazole series and study their physicochemical properties.

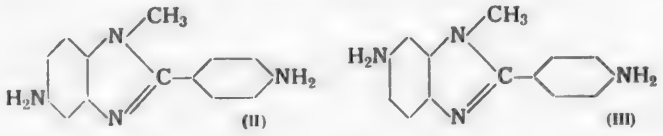
The diamines of this series, as could be postulated on the basis of theoretical considerations and literature information, when diazotized and subjected to azo coupling, should give substantive dyes.

Little mention has been made in the literature relative to diamines of the benzimidazole series, and consequently it was necessary to develop a method for their preparation. It proved that the indicated diamines were easily synthesized by conventional methods (see experimental section).

6(5)-Amino-2-p-aminophenylbenzimidazole (I), containing the imidazole ring, is a close analog of benzidine. Due to tautomerism, this diamine can have a second structure.

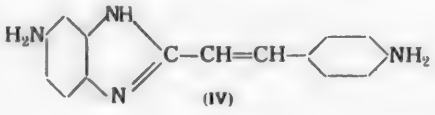


As can be seen from the formulas, the second tautomer fails to show conjugation between the amino groups. To determine which tautomer predominates in the usually obtained mixture, it was necessary to compare the properties of the latter with the properties of the two isomers (II) and (III) shown below.

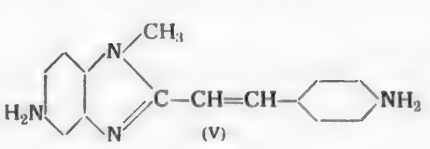


Judging by the similarity and difference in the properties, it becomes possible to arrive at a decision as to the structure of diamine (I).

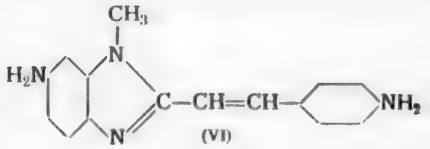
Further, in order to follow the substantive properties shown by azo dyes derived from the diamines, it seemed of interest to lengthen the system of conjugated double and single bonds and to introduce the additional vinyl grouping between the terminal groups, i. e., the synthesis of diamine (IV) seemed in order.



In the same manner as before, this diamine should be compared with the analogous methylated diamines (V) and (VI), also differing from each other by the presence or absence of conjugation between the amino groups.

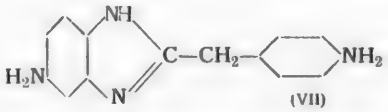


(V)



(VI)

In addition, it seemed of interest for the same reason to study the effect of introducing some other group, known to interrupt conjugation, in place of the vinyl grouping, for example, the methylene group (VII).



(VII)

Since most of the contemporary theories on substantivity associate this property with the presence of a conjugated system in dye molecules, and since, on the other hand, the reciprocal influence shown by amino groups in diamine molecules also depends on this conjugation, it was postulated that having studied the degree of conjugation found in diamine molecules, it then becomes possible to compare it with the magnitude of substantitivity shown by the azo dyes derived from the studied diamines. In our opinion, the degree of conjugation found in diamine molecules should be reflected on the values of their dissociation constants. For this reason we give the results of a physicochemical study of the above-mentioned diamines in this paper.

Basicity Constants of Synthesized Diamines

No. of diamine	$k_1 \cdot 10^{8}$	$k_2 \cdot 10^{11}$	$k_3 \cdot 10^{12}$
(I)	2.34	1.29	2.82
(II)	4.47	1.1	2.76
(III)	2.63	1.18	2.89
(IV)	1.99	1.63	3.52
(V)	3.99	1.91	3.99
(VI)	1.48	1.12	3.02
(VII)	1.82	6.03	6.31

Study of the principal properties of diamines of the benzimidazole series. The relationship between the reactivity of aromatic amines and their basicity constants in acylation and diazotization reactions, and in the formation of azomethines, diazo compounds and imidazole derivatives, was investigated earlier [1].

We decided to continue these studies in the direction of investigating the relationship that exists between the basicity constants of the diamines synthesized by us and their structure. The question as to the interrelationships existing between the basicity constants of the diamines (first and second), the degree of simultaneous diazotization shown by the two amino groups, etc. is an extremely complex one, and is of great theoretical and practical interest.

In the cases studied by us the relationship between the basicity constants and the structure is made even more complicated by the fact that the examined products have three basicity constants. Since for most of the studied diamines the first basicity constant is more or less constant, and at the same time is close to the value of the basicity constant of benzimidazole ($k \approx 1 \cdot 10^{-9}$), then obviously this constant should be regarded as belonging to the imidazole ring.

Consequently, the second and third constants should be regarded as belonging to the amino groups of the diamines studied by us. The potentiometric titration method was used to determine the basicity constants. The experimental results obtained by us are given in the table.

A comparison of the basicity constants of diamines (I) and(IV) with those of their alkyl derivatives could possibly give an answer to the question of the structure of diamines (I) and (IV). However, due to the greater basicity of the imidazole ring in comparison to the amino groups, it is the first to be involved in salt-formation. This salt-formation destroys the difference between the alkyl isomers, as a result of which the basicity constants of the amino groups in both the isomeric diamines and diamines (I) and (IV) are extremely close to each other.

Since these constants differ but slightly from the corresponding constants of diamine (VII), in which the presence of a methylene group is known to interrupt conjugation between the two amine groups, it must be assumed that salt-formation involving the imidazole ring leads in all cases to disruption of conjugation between the amino groups.

EXPERIMENTAL

Synthesis of 6-amino-2-p-aminophenylbenzimidazole. A mixture of 45 g of dinitroaniline and 45 g of p-nitrobenzoyl chloride was melted in a reaction flask in an oil bath at 180° [2]. Here hydrogen chloride was evolved copiously. Toward the end of reaction the temperature was raised to 200°; the temperature of the mass was held here for 15 min. On conclusion of reaction the obtained product was washed with acetone to remove starting substances and tarry products. Recrystallization from pyridine gave pale yellow needles of 2,4-dinitro-1-p-nitrobenzoylaniline with m. p. 195°. The yield was 70 g (81.4%).

2,4-Dinitro-1-p-nitrobenzoylaniline (43 g) was added gradually (reaction is vigorous) to a boiling solution of stannous chloride in 250 ml of hydrochloric acid (d 1.19). The reaction mass on cooling deposited the complex of the diamine with stannous chloride, which was filtered and dissolved in water. The tin was precipitated electrolytically. The precipitate, obtained by evaporation of the solution, was dissolved in a small amount of water and precipitated with ammonia. Recrystallization from water gave 6-amino-2-p-aminophenylbenzimidazole. M. p. 235-236° [2]. Yield of product 20.5 g (74%). The molecular weight of the 5(6)-amino-2-p-aminophenylbenzimidazole was determined by potentiometric titration and proved to be 223.1 (calculated 224).

Synthesis of 5-amino-1-methyl-2-p-aminophenylbenzimidazole. We synthesized 2,4-dinitrodimethylaniline by the Schuster method [3]. To oxidize this product to 2,4-dinitromethylaniline we used the Romburgh method [4], which consisted in treating the compound with chromic anhydride in acetic acid at the boil (for 1 part of 2,4-dinitrodimethylaniline we took 4 parts of glacial acetic acid and 1 part of chromic anhydride; reaction time 30-40 min, and yield 57.2%).

The obtained product was partially reduced to 4-nitro-2-aminomethylaniline by analogy with the reduction of 2,4-dinitroaniline, according to [5], i. e., by reduction with hydrogen sulfide in alcoholic ammonia medium. The yield of product was 64.8%. M. p. 177° (from alcohol). The obtained 2-amino-4-nitromethylaniline was converted to the imidazole derivative by condensation with p-nitrobenzoyl chloride in the following manner. A previously blended mixture of 15 g of 4-nitro-2-aminomethylaniline and 15 g of p-nitrobenzoyl chloride was placed in a porcelain beaker. The reaction mass was gradually heated in an oil bath to 170-180°. At 90° the mixture changed from a red to a yellow color, which apparently could be due to progress of acylation. Water began to be evolved at 160°, which indicates closure of the ring. The yield of 5-nitro-1-methyl-2-p-nitrophenylimidazole was 25.5 g (96%). It was obtained as yellow needles after recrystallization from pyridine. M. p. 272-273°.

Found %: N 18.99, 19.05. $C_{14}H_{10}O_4N_4$. Calculated %: N 18.79.

The obtained product was reduced in the same manner as in the previous case. To synthesize 5-amino-1-methyl-2-p-aminophenylbenzimidazole we took 10 g of 5-nitro-1-methyl-2-p-nitrophenylbenzimidazole, 140 g of stannous chloride and 100 ml of concentrated hydrochloric acid. The yield of 5-amino-1-methyl-2-p-aminophenylbenzimidazole was 7.1 g (88.5%). The product was purified by precipitation from hydrochloric acid with ammonia, followed by recrystallization from water. The product was obtained as brown needles. M. p. 203-204°.

Found %: N 23.62, 23.56. M (potentiometric) 233. $C_{14}H_{14}N_4$. Calculated %: N 23.53. M 238.

Synthesis of 6-amino-1-methyl-2-p-aminophenylbenzimidazole. The nitration was run by the Fitch method [6], and the oxidation by the Romburgh method, the latter in the same manner as had been described for the oxidation of 2,4-dinitrodimethylaniline. A mixture of 13 g of 2,5-dinitromethylaniline and 13 g of p-nitrobenzoyl chloride was blended by grinding in a mortar. The obtained mixture was fused in a porcelain beaker at 140°. On conclusion of reaction the yellow powder was isolated, and recrystallized from alcohol. Yield 25.5 g (81%). 2,5-Dinitro-1-methyl-1-p-nitrobenzoylaniline has m.p. 146°.

Found %: N 16.17, 16.25. $C_{14}H_{10}O_7N_4$. Calculated %: N 16.18.

The obtained product was reduced to 6-amino-1-methyl-2-p-aminophenylbenzimidazole by the above-described procedure. For the synthesis we took 18.9 g of 2,5-dinitro-1-methyl-1-p-nitrobenzoylaniline, 232 g of stannous chloride and 150 ml of hydrochloric acid (d 1.18). The yield of 6-amino-1-methyl-2-p-aminophenylbenzimidazole as the free base was 9.1 g (66.5%). The product was purified by recrystallization from water. M. p. 231°.

Found %: N 23.70, 23.72. $C_{14}H_{14}N_4$. Calculated %: N 23.53.

Synthesis of 5-amino-1-methyl-2-p-aminostyrylbenzimidazole. A mixture of 18 g of 5-nitro-1,2-dimethylbenzimidazole and 18 g of p-nitrobenzaldehyde, previously blended in a mortar, was placed in a porcelain beaker. The reaction mixture was heated in an oil bath to 180°. Water soon began to be evolved, which indicated the start of condensation. The liquid melt became solid toward the end of reaction. To complete the reaction the temperature was raised to 200°. The obtained hard melt was then ground to a powder. Yield of 5-nitro-1-methyl-2-p-nitrostyrylbenzimidazole 31 g (83.4%). M. p. 262°. After recrystallization from pyridine, m. p. 278°.

Found %: N 17.03, 17.29. $C_{16}H_{12}O_4N_4$. Calculated %: N 17.26.

Into a liter flask, fitted with stirrer and condenser, was charged 300 ml of alcohol, 300 ml of hydrochloric acid (d 1.19), 225 g of stannous chloride and 28.5 g of 5-nitro-1-methyl-2-p-nitrostyrylbenzimidazole. The solution was heated to the boil and heated under reflux for 3 hrs. The precipitate gradually disappeared. At the end of reaction the solution was cooled, and the deposited complex salt of diamine with stannous chloride was filtered and then dissolved in water. The tin was precipitated electrolytically. The solution was evaporated to dryness. The residue was then dissolved in a small volume of water and precipitated with ammonia. The yield of 5-amino-1-methyl-2-p-aminostyrylbenzimidazole was 14.3 g (61.9%). After repeated precipitation of the diamine hydrochloride with ammonia the melting point of the free base rose to 218-219°.

Found %: N 21.06, 21.01. M (potentiometric) 272. $C_{16}H_{16}N_4$. Calculated %: N 21.20. M 264.

Synthesis of 1,2-dimethyl-6-nitrobenzimidazole.* 1,2-Dimethyl-6-nitrobenzimidazole was synthesized by the Phillips scheme [7], which we had studied in detail. 2-Methyl-5(6)-nitrobenzimidazole (190 g) was heated in methyl alcohol, containing hydrogen chloride in an amount equal to 75% of the benzimidazole. The reaction was run for 4 hrs at 160°. At the end of reaction the mass was treated with ammonia to separate from quaternary derivative, and then with alkali to remove starting product. We obtained 35 g of crude product. Recrystallization from alcohol raised the melting point to 195-210°, and then recrystallization from nitrobenzene raised it to 220-225°. The product was recrystallized 4 times. We obtained 7.5 g of 1,2-dimethyl-6-nitrobenzimidazole with m. p. 252-252.5° [7]. A mixture of this compound with the other pure isomer (5-nitro-1,2-dimethylbenzimidazole), having m. p. 225-226° (literature gives 226°), melted at 195-222°.

Found %: N 21.93, 22.13. $C_9H_9O_2N_3$. Calculated %: N 21.99.

Synthesis of 6-amino-1-methyl-2-p-aminostyrylbenzimidazole. For this synthesis we used the method described by A. E. Porai-Koshits [8] and O. Kym [2] for the synthesis of similar compounds. A mixture of 7 g of 1,2-dimethyl-6-nitrobenzimidazole and 7 g of p-nitrobenzaldehyde was placed in a reaction test tube and heated in an oil bath to 180°. Complete melting of the mass occurred at this temperature. The condensation reaction began at the same time, the start of which could be judged by the droplets of water collecting on the walls of the test tube. After holding at this temperature for 30 min the temperature was gradually raised (in 30 min) to 210°. As soon as the liquid melt turned solid, further heating could be stopped. Then the cooled dark-brown melt was ground to a powder and boiled with alcohol to remove unreacted starting substances. Yield of crude product 11.1 g (93.5%). M. p. 280-281°. The synthesized dinitro derivative is a bright yellow, finely crystalline compound that is insoluble in ether, alcohol, acetone and nitrobenzene. Recrystallization from hot pyridine gave 10.45 g of 6-nitro-1-methyl-2-p-nitrostytylbenzimidazole, m. p. 282.5-283.5°.

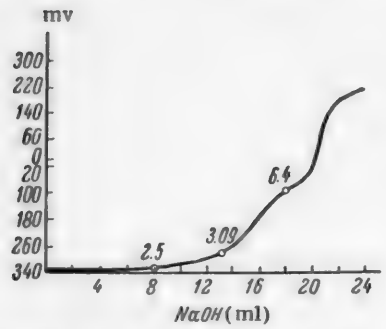
Found %: N 17.32, 17.45. $C_{16}H_{12}O_4N_4$. Calculated %: N 17.26.

The obtained dinitro derivative was then reduced with stannous chloride in a mixture of alcohol and hydrochloric acid by the method described above for the reduction of 5-nitro-1-methyl-2-p-nitrostyrylbenzimidazole. For the reduction we took 6 g of 6-nitro-1-methyl-2-p-nitrostyrylbenzimidazole. The reduction solution on cool-

* The compound was synthesized by graduate student E. Zonis.

ing and long standing deposited the complex salt of the diamine with tin (1st portion). Evaporation of the filtrate gave some more of the tin complex (2nd portion). Both portions of complex salt (each separately) were then dissolved in water, and the tin was precipitated electrolytically at a copper electrode (carbon anode). The solution, containing the diamine hydrochloride, was evaporated to dryness. Evaporation of the 1st portion yielded 5.6 g of the salt, while the 2nd portion yielded 3.4 g. Evidently the hydrochloride contains water of crystallization. Recrystallization from water, using bone charcoal for decolorization, gave 2.2 g of bright orange salt. The filtrates were collected, evaporated to dryness, and the residue was recrystallized from concentrated hydrochloric acid; another 3.8 g of salt was isolated here. The obtained salt does not melt even when heated to 340°, but only darkens. To obtain the free base a solution of the salt was treated with ammonia. Due to the fact that the diamine is easily oxidized, the solution of the salt was treated with hydrogen sulfide prior to precipitation with ammonia. To effect complete decomposition of the salt the solution was boiled with excess ammonia; 6-amino-1-methyl-2-p-aminostyrylbenzimidazole was obtained as a bright yellow product with m. p. 212-214°.

Found %: N 21.48, 21.13. M (potentiometric titration) 265. $C_{16}H_{16}N_4$. Calculated %: N 21.2. M 264.



Synthesis of 5(6)-amino-2-p-aminobenzylbenzimidazole. A mixture of 13 g of 2,4-dinitroaniline and 15 g of p-nitrophenylacetyl chloride was blended thoroughly and then melted in a reaction beaker at 120-140°. The reaction was run for about an hour. The resulting dark melt was then ground in a mortar. The yield of 2,4-dinitro-1-p-nitrophenylacetylaniline was 24.2 g (97.6%). Recrystallization from pyridine gave yellow crystals. M. p. 175°.

Found %: N 16.22, 16.19. $C_{14}H_{10}O_7N_4$. Calculated %: N 16.18.

The above-described procedure was used to reduce the obtained product to 6-amino-2-p-aminobenzylbenzimidazole. For the reduction we took 20 g of 2,4-dinitro-1-p-nitrophenylacetylaniline. The yield of free base was 8.7 g (48.7%). 6-Amino-2-p-aminobenzylbenzimidazole was reprecipitated several times from hydrochloric acid with ammonia, followed by recrystallization from water. The pure product has m. p. 223°.

Found %: N 23.40, 23.30. M (potentiometric) 246. $C_{14}H_{14}N_4$. Calculated %: N 23.5. M 238.

Potentiometric titration of the diamines—benzimidazole derivatives. A solution of 0.1 g of diamine in a mixture of 37.5 ml of ethyl alcohol and 37.5 ml of water was treated with 10-15 ml of 1 N hydrochloric acid. The solution prepared in this manner was titrated with 0.0952 N sodium hydroxide solution using an LP-4 potentiometer with glass electrode. In all cases the titration curve had two inflection points; one corresponded to titration of the excess hydrochloric acid, and the other corresponded to titration of the benzimidazole itself.

Calculation of the basicity constants, given in the table, was made from the semiequivalent points. As an example we have shown the potentiometric titration curve of 6-amino-2-p-aminophenylbenzimidazole (see figure).

SUMMARY

Diamines of the benzimidazole series, containing two amino groups in different benzene rings, have close basicity constants, independent of whether the amino groups are or are not found in conjugation. The reason for this phenomenon must be sought in the greater basicity of the imidazole ring when compared to the amino groups, as a result of which it is the first to be involved in salt-formation, and its transformation here into the onium ion leads to rupture of the conjugation between the amino groups.

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DIAMINES OF BENZIMIDAZOLE SERIES

II. SUBSTANTIVE PROPERTIES OF THE AZO DYES DERIVED FROM THE DIAMINES

B. A. Porai-Koshits and Ch. Frankovskii

The affinity of dyes for fibers (substantivity) is quite a complex phenomenon, depending on many factors: the chemical structure of the dye and its physical properties, the nature of the fiber, the dyeing conditions, etc. According to a number of authors [1-4], one of the most important substantivity factors is the chemical structure of the dye, in particular, the length of the chain of conjugated bonds and the coplanarity of the molecule.

In studying the problem of the relationship between substantivity and coplanarity it has been impossible to determine by physical measurements whether coplanarity is present or absent; here the investigators have limited themselves only to theories, analogies, etc. Up to now it has not been conclusively shown that an angle exists between the two phenyl groups in benzidine. For substituted benzidines, a priori, it has been assumed without experimental proof that bulky substituents, introduced in the 2,2'-positions, take the benzene rings out of one plane [4]; the electronic effect of these substituents was not taken into consideration here, which in itself, independent of whether the molecule has a planar or a nonplanar structure, can shorten the chain length of the conjugated bonds to varying degree.

The present paper is a continuation of the investigations made by A. E. Porai-Koshits in the domain of substantive benzimidazole dyestuffs. In the opinion of A. E. Porai-Koshits, the benzimidazole ring is a strong chromophore, enhancing the substantive properties of a dye molecule. Consequently, it could be expected that benzimidazole dyestuffs will show quite high substantivity. In the previous communication [5] we described seven diamines of this series, defined their structure, and determined their basicity constants.

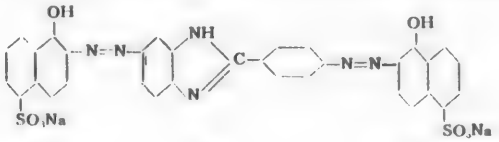
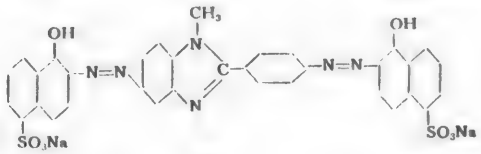
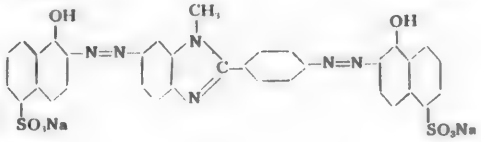
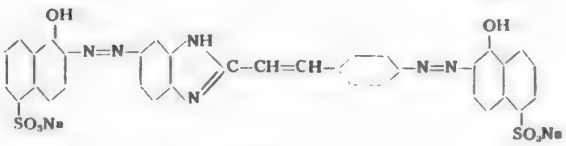
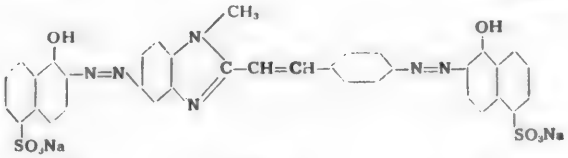
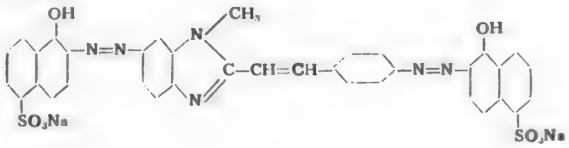
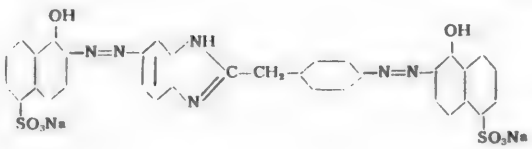
The direct purpose of the present study was to synthesize the azo dyes derived from the investigated diamines and study their substantivity properties. We took 1,5-naphthosulfonic acid as the azo component, and for some of the dyes we took naphthnoic, H-, J-, and Chicago-SS acids. Based on these examples, we followed the effect of diamine structure on the substantive properties of the dyes, and also the effect of the azo component on them.

The results of our experiments are summarized in Tables 1 and 2.

As we had already mentioned in the previous communication [5], the principal difference between the synthesized diamines of the benzimidazole series consists in the fact that some of them have conjugated chains of double and single bonds, and some do not have them. Thus, 6-amino-1-methyl-2-p-aminophenylbenzimidazole and 6-amino-1-methyl-2-p-aminostyrylbenzimidazole show an uninterrupted chain of double and single bonds between the amino groups, while in the diamines 5-amino-1-methyl-2-p-aminophenylbenzimidazole and 5-amino-1-methyl-2-p-aminostyrylbenzimidazole this chain is absent; finally, the diamines 5(6)-amino-2-p-aminophenylbenzimidazole and 5(6)-amino-2-p-aminostyrylbenzimidazole, because of possible isomerization, may or may not contain conjugated chains. Actually, the presence or absence of conjugation in the azo dyes synthesized by us from all of the above-enumerated diamines exerts a sharp influence on their substantivity values; thus, dye (III) proved to be more substantive than dye (II), and very close to dye (I) in its affinity value (see Table 1). The same also holds for the styryl derivative of benzimidazole; dyes (IV) and (VI) (see Table 1) proved to be more substantive than dye (V); here it should be mentioned that the substantivity of the styryl derivatives is greater than that of the phenyl derivatives of benzimidazole, since they possess a longer conjugation chain (compare dyes (IV) and (I), (V) and (II), and (VI) and (III); Table 1).

TABLE 1

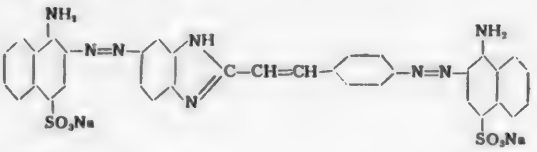
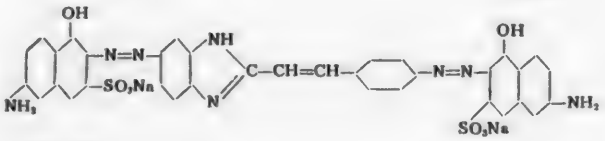
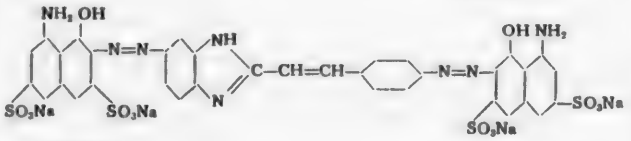
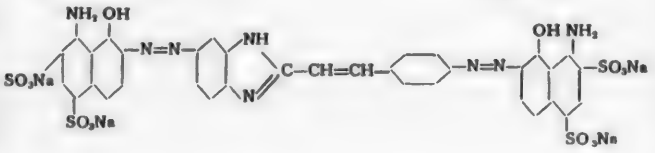
Substantivity Values of Synthesized Dyes

Nos. of dyes	Dye	Substantivity (in %)
(I)		38
(II)		18
(III)		30
(IV)		40.8
(V)		24
(VI)		48
(VII)		10.3

• The dyeings were made according to the method of D. G. Perelaslova (in the presence of soda and salt).

TABLE 2

Substantivity Values of Synthesized Dyes

Nos. of dyes	Dye	Substantivity (in %)	
		A*	A**
(I)		9	53
(II)		27	—
(III)		9	66
(VI)		6.5	40

* The dyeings were made according to the method of B. M. Bogoslovskii (in the absence of salt).

** The dyeings were made according to the method of D. G. Pereiaslova (in the presence of soda and salt).

As was to be expected, dye (VII), in which conjugation is broken by the introduction of a methylene group, proved to be much less substantive than dyes (I), (III), (IV) and (VI), the latter all possessing an uninterrupted chain of conjugated single and double bonds.

As regards dyes (I) and (IV), then based according to their substantivity values, they closely resemble dyes in which a long system of conjugated bonds exists. From this it can be concluded that in the indicated dyes the hydrogen atom of the benzimidazole ring is linked to the nitrogen not found in the conjugation chain. Apparently, a similar conclusion should be made regarding the original diamines themselves. We shall mention that a study of the basicity constants of 5(6)-amino-2-p-aminophenylbenzimidazole and 5(6)-amino-2-p-aminostyrylbenzimidazole failed to give us an answer to the structure of these diamines, which can vary because of tautomerism [5]. Consequently, determining the substantive properties of the azo dyes apparently proved to be a more precise study method, since it also permitted arriving at a conclusion as to the structure of the original diamines.

The above-enumerated facts indicate that a rule, similar to that observed for dyes of the benzidine series, also holds in the series of benzimidazole dyes. The character of the influence exerted by different azo-components on the substantivity value of a dye is also retained in going from the benzidine to the benzimidazole series. The dyes derived from J-acid are more substantive than the dyes derived from H-acid, while the dyes derived from H-acid are more substantive than the dyes derived from Chicago-SS acid (see Table 2). The question of the influence exerted by the sulfo group on substantivity must be considered unsolved.

EXPERIMENTAL

The dyes were synthesized in conventional manner. The obtained amines were diazotized with sodium nitrite solution in hydrochloric acid medium. For example, for a typical reaction we took 2.5 g of 6-amino-2-p-aminostyrylbenzimidazole, 30 ml of water, 4 ml of hydrochloric acid, and 1.4 g of sodium nitrite in 4 ml of water. The azo coupling was run in alkaline medium, as described below.

A mixture of 5 g of azurinic acid and 6.75 g of soda was dissolved in 50 ml of water; the obtained solution was cooled to 0°. The above-obtained diazo solution was added to this solution with constant stirring, keeping the temperature at 0-5°. The reaction course was controlled by means of either excess diazo-component or azo-component. To complete azo-coupling the reaction mass was stirred for 3 hrs. At reaction end all of the dyestuff was found as sodium salt in the precipitate. The filtrate had a slight yellow-green color, and further salting out failed to yield any more dyestuff.

The purity of the obtained dye was controlled chromatographically. The presence of any other dyes could not be shown. The dye was filtered and dried at 105°. The yield of technical product was 8.7 g. The benzidine method, first proposed by B. M. Bogoslovskii [4], was used to purify the dyestuff. The dyestuff was dissolved in water, heated to the boil, and then a hot solution of benzidine hydrochloride was added. This gave the salt of the dyestuff with benzidine as a precipitate, which was filtered and washed with cold water until the test for chloride ion was negative. After this the salt of the dye with benzidine was dried and weighed. The obtained salt was heated in soda solution for 20 min. The amount of soda used was calculated in advance; it was not more than 80% of the amount theoretically required to decompose the salt. Here the benzidine and traces of the benzidine salt of the dye deposited in the precipitate, while the dye remained in solution as the sodium salt. The solution was filtered through a fluted filter and then evaporated to dryness.

The dyes were analyzed by titration with titanium trichloride.

A 0.1 g sample of the dye was dissolved in 250 ml of water. Then a 50 ml aliquot of the solution was removed with a pipette, the aliquot treated with 25 ml of a 20% Rochelle salt solution, and the whole heated to the boil. The boiling solution was titrated with 0.0282 N $TiCl_3$ to the appearance of a yellow color (or decolorization), with constant passage of carbon dioxide through the solution. The excess titanium chloride was back-titrated with methylene blue solution. The results were calculated according to the procedure given in [7].

The purity of some of the dyestuffs was also controlled by the use of benzidine hydrochloride and by microanalysis for elemental sulfur. The substantivity was determined as the difference between the starting and final dye bath. We used the method of B. M. Bogoslovskii to make the dyeings: weight of cloth sample 1 g, concentration of sodium chloride solution 5 g/liter, amount of dye 4% on weight of cloth, bath ratio 1:40, time of dyeing 1 hr. Since some of the dyes coagulated under these conditions, we also used the dyeing method of D. G. Pereiaslova [6]: 1 g of cloth, amount of dye 0.00002 mole, 2% soda and 20% sodium chloride on weight of cloth, bath ratio 1:30, time of dyeing 1 hr, temperature 80°. Parallel experiments with blank baths containing only the dye solutions were run at the same time. The substantivity was expressed in percent of dyestuff absorbed. The concentrations of the dye baths were determined using both the colorimetric method and the method of titration with titanium trichloride.

SUMMARY

The dyes, formed from bis-diazotized diamines of the benzimidazole series and 1,5-naphtholsulfonic acid, show different substantivity depending on whether the azo groups are or are not in mutual conjugation. Based on the substantivity values of the obtained azo dyes it becomes possible to judge whether conjugation is present or absent between the amino groups of the original diamines taken for synthesis of the indicated dyes. The character of the influence exerted by other azo-components (for example, J-, H- or Chicago-SS acid) on the substantivity of the azo dyes discussed here is similar to that exerted in the benzidine dye series.

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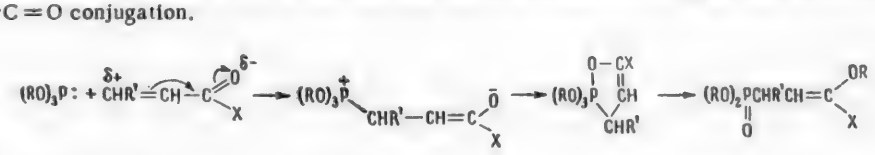
** Original Russian pagination. See C. B. translation.

ADDITION OF NEUTRAL ESTERS OF PHOSPHOROUS AND PHOSPHONOUS ACIDS TO CONJUGATED SYSTEMS

IV. ADDITION OF ESTERS OF PHENYLPHOSPHONOUS ACID TO α,β-UNSATURATED ALDEHYDES AND ACIDS

Gil'm Kamai and V. A. Kukhtin

In earlier communications [1] we described the reaction between trialkyl phosphites and compounds showing C=C−C=O conjugation.

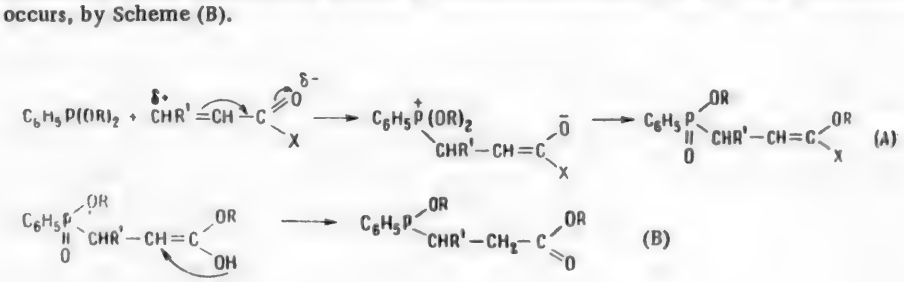


This reaction in its mechanism is similar to the reaction of alkyl halides with trialkyl phosphites, and can be regarded as one of the forms of the Arbuzov rearrangement.

It could be expected that the esters of phenylphosphonous acid, reacting with alkyl halides and being more active than the trialkyl phosphites, would easily react with conjugated systems.

As our experiments revealed, the esters of phenylphosphonous acid actually do react very vigorously with α,β-unsaturated aldehydes and acids. Reaction here is much more vigorous than in the case of the trialkyl phosphites. Thus, for example, the esters of phenylphosphonous acid react with methacrylic acid with the evolution of heat, in which connection the temperature rises to 125-130° when the reactants are poured together slowly. The reaction with acrylic acid and with acrolein is even more vigorous. The addition products of phenylphosphonous esters to acrolein lend themselves with great difficulty to distillation even in a high vacuum; in this connection we were able to isolate only the addition product of the ethyl ester of phenylphosphonous acid to acrolein in the pure state. Since the reaction of α,β-unsaturated aldehydes and acids with phenylphosphonous esters proceeds more violently than in the case of the trialkyl phosphites, and is accompanied by a much greater evolution of heat, we were unable to confirm, even indirectly, the presence of an intermediate product in the Arbuzov rearrangement.

It is possible to depict the reactions studied by us by Scheme (A), and in the case of acids, where hydrogen migration occurs, by Scheme (B).



The constants of the ethyl ester of β-phenylphosphonoisobutyric acid obtained by us lie close to those described earlier by A. N. Pudovik [2].

The results obtained by us indicate that the conclusions of A. E. Arbuzov [3] relative to the reactivity of different esters of trivalent phosphorus with alkyl halides are also valid for other cases of the Arbuzov rearrangement, in particular, also for the case where systems with C=C−C=O conjugation are involved.

The constants of the compounds synthesized by us are given in the table.

Expt. nos.	Formula	Boiling point (pressure in mm)	n_D^{20}	d_0^{20}	%P		Yield (in %)
					calc.	found	
1	$C_6H_5P(O)(OCH_3)CH_2CH_2COOCH_3$	159—160° (5)	1.5062	1.1591	12.81	12.63	40.4
2	$C_6H_5P(O)(OC_2H_5)CH_2CH_2COOC_2H_5$	178—179 (3)	1.5040	1.1532	11.48	11.42	51.5
3	$C_6H_5P(O)(OC_3H_7\text{-}n)CH_2CH_2COOC_3H_7\text{-}n$	183—184 (5)	1.4995	1.0691	10.32	10.01	50.3
4	$C_6H_5P(O)(OCH_3)CH_2CH(CH_3)COOCH_3$	163—165 (5)	1.5046	1.1297	12.07	11.83	38.0
5	$C_6H_5P(O)(OC_2H_5)CH_2CH(CH_3)COOC_2H_5$	185—186 (8)	1.5000	1.1210	10.91	10.65	40.2
6	$C_6H_5P(O)(OC_3H_7\text{-}n)CH_2CH(CH_3)COOC_3H_7\text{-}n$	188—190 (9)	1.5019	1.1261	9.93	9.68	32.5
7	$C_6H_5P(O)(OC_2H_5)CH_2CH{=}CHOC_2H_5$	150—152 (0.5)	1.5136	1.0389	12.18	11.88	11.2

EXPERIMENTAL

Addition of ethyl ester of phenylphosphonous acid to methacrylic acid. 10 g of ethyl phenylphosphonite was treated with 4.4 g of methacrylic acid. The temperature of the mixture quickly rose to 130°; to prevent further temperature rise the reaction flask was cooled with ice water. The reaction mass was cooled to room temperature and then heated for 1 hr at 130-134°. Vacuum-distillation gave 6.2 g (40.2%) of the ethyl ester of β-phenylphosphonoisobutyric acid.

B. p. 185-186° (8 mm); $n^{20}D$ 1.5000, d^{20}_0 1.1210, MR_D 74.50; calculated 74.12. Found %: P 10.65. $C_{14}H_{21}O_4P$. Calculated %: P 10.21.

The reaction with other esters of phenylphosphonous acid was run in a similar manner. The reaction with acrylic acid proceeds more violently and requires stronger cooling.

Addition of the ethyl ester of phenylphosphonous acid to acrolein. The reaction was run in dioxane.

3 g of acrolein was added with cooling in drops to a solution of the phenylphosphonous ester. The temperature during reaction was kept at 80-100°. Vacuum-distillation gave 1.4 g of the ethyl ester of γ-ethoxyallylphenylphosphonous acid.

B. p. 150-152° (0.5 mm); $n^{20}D$ 1.5136, d^{20}_0 1.0389. Calculated %: P 12.18. $C_{13}H_{19}O_3P$. Found %: P 11.88.

SUMMARY

The reaction between the esters of phenylphosphonous acid and α,β-unsaturated aldehydes and acids was studied. It was established that the esters of phenylphosphonous acid add to α,β-unsaturated aldehydes and acids in the same manner as the trialkyl phosphites.

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* Original Russian pagination. See C. B. translation.

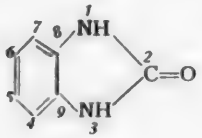
** In Russian.

IMIDAZOLE DERIVATIVES

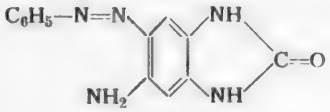
XX. SOME AMINO DERIVATIVES OF BENZIMIDAZOLONE

L. S. Efros and A. V. El'tsov

In studying the chemical properties of amino derivatives of benzimidazolone (I) we established [1] that the azo coupling of 5-aminobenzimidazolone with diazotized aniline takes place at carbon 6 of (II); 5-amino-1,3-dimethylbenzimidazolone behaves in exactly the same manner.



(I)



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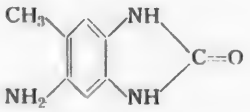


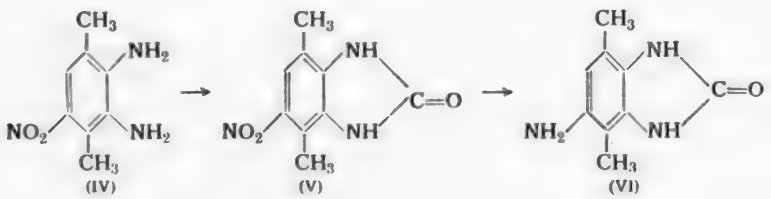
(III)

On the basis of this we postulated that under the influence of the imidazolone ring the electron cloud of the benzene ring in benzimidazolone is deformed in such manner that the double-bond character between carbon atoms 5 and 6 is greatly increased.

In order to determine the degree of this deformation we decided to synthesize two aminobenzimidazolones, one of which had the 6 position, and the other the 4 position, blocked by a methyl group, and to determine how these compounds would react with diazonium salts.

Starting with the earlier described [2] 6-methyl-5-nitrobenzimidazolone we synthesized 5-amino-6-methylbenzimidazolone (III), which failed to enter into azo coupling with all of diazo compounds tested by us, clear up to p-nitrophenyldiazonium chloride, and the solitary reaction product always proved to be the diazoamino compound.

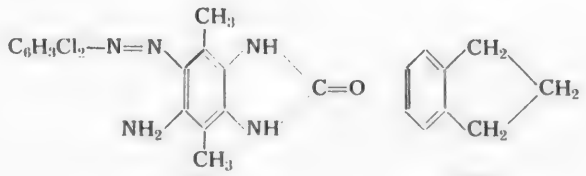
As the amine in which the carbon atom in position 4 was blocked we used 5-amino-4,7-dimethylbenzimidazolone (VI), synthesized by the scheme



The starting 1,2-diamino-3,6-dimethyl-4-nitrobenzene (IV) was obtained earlier by the reduction of 2,4-dinitro-3,6-dimethylbenzazide [3]. The cited authors state that the same diamine can also be obtained by the partial reduction of 2,4-dinitro-3,6-dimethylaniline [4]. We employed the last method, running the reduction with sodium sulfide in alcohol medium. Treatment of diamine (IV) with carbon bisulfide in alkaline alcoholic medium gave us 4,7-dimethyl-5-nitro-2-mercaptobenzimidazole. The fusion of diamine (IV) with urea proceeds

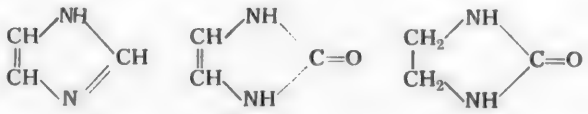
very smoothly and if (IV) is sufficiently pure the obtained nitro compound can be reduced without purification by recrystallization.

As we had anticipated, 5-amino-4,7-dimethylbenzimidazolone (VI) readily entered into azo coupling with diazotized aniline and 2,5-dichloroaniline; the last azo dye was purified and analyzed (VII). These facts serve as convincing evidence that in the benzene ring of benzimidazolone the double-bond linkage of positions 5-6 is substantially increased, while that of positions 4-5 and 6-7 is correspondingly decreased. Such a disruption of bond equality was postulated earlier only for the case of hydrindene (VIII) [5]; however, it was shown in later papers that this postulation is incorrect [6]. For this reason the observations presented by us here deserve special attention, while the conclusions derived from them deserve further experimental verification by both chemical and physical methods.



(VII) (VIII)

To explain the imidazolone ring exerting such an influence on the benzene ring condensed with it, it is expedient to compare the chemical properties of imidazole (IX) and imidazolone (X) [7]. The first compound is characterized by having a clearly defined aromatic nature, whereas the second compound tends to migrate into derivatives of imidazolone (XI), adding hydrogen, halogens, etc.



(IX) (X) (XI)

The presence of a system of 6 π-electrons in imidazole (IX) and the absence of the same in imidazolone (X) leads to the situation that these heterocycles exert different influence on the benzene rings condensed with them. Imidazolone, striving to assume the more stable structure of imidazolidone (XI), in the benzo derivatives "forces out" the π-electrons of bonds 8-9 into the benzene ring (I), which leads to the manifested disruption of the equality of the bonds in the benzene ring of benzimidazolone. Imidazole strives to retain its aromatic structure, which is reflected in a "naphthalene-like" deformation of the electron cloud of the benzene ring in benzimidazole [8].

EXPERIMENTAL

2,4-Dinitro-3,6-dimethylaniline. A mixture of 70 g of trinitro-p-xylene and 1600 ml of alcohol was charged into a flask, fitted with reflux condenser and a tube for bubbling in gas, descending to the bottom of the flask. A fast stream of ammonia was passed through the solution for 3 hrs with simultaneous heating on the water bath. Then the mixture was heated for another hour at the boil, and then cooled. The obtained crystalline precipitate was filtered, washed on the filter with a small amount of alcohol, and dried. The crude product melts at 201° and can be used for subsequent work without further purification. Yield 65-70%. After one recrystallization from acetic acid the coarse yellow needles of 2,4-dinitro-3,6-dimethylaniline melted at 203°.

1,2-Diamino-3,6-dimethyl-4-nitrobenzene. A mixture of 12.3 g of finely divided 2,4-dinitro-3,6-dimethylaniline and 100 ml of alcohol was placed in a flask, fitted with stirrer, reflux condenser, thermometer and dropping funnel, and to this mixture at 55° and with vigorous stirring was added in drops a warm solution of 22 g of crystalline sodium sulfide in 20 ml of water at such a rate that the temperature did not exceed 65°. The addition of the sodium sulfide solution was accompanied by a rise in temperature; however, in some cases additional heating was required to initiate reaction. After all of the reducing agent had been added, the mixture was stirred vigorously at 65-70° for 15 min, and here the 2,4-dinitro-3,6-dimethylaniline went into solution. Then the dark-red

solution was poured into a porcelain dish, acidified with hydrochloric acid until acid to Congo, and then evaporated on the water bath to dryness. The dry residue was treated twice with 100-ml portions of boiling dilute hydrochloric acid, the precipitate was filtered, and the mother liquors were neutralized with ammonia. The obtained precipitate of diamine was filtered, for purification was reprecipitated twice from dilute hydrochloric acid with ammonia, and then dried. Yield 4-6.3 g. The product melts at 166° and can be used without further purification. One recrystallization from alcohol gave the diamine with m. p. 169°, which agrees with the literature [3].

4,7-Dimethyl-5-nitrobenzimidazolone. A mixture of 5.8 g of 1,2-diamino-3,6-dimethyl-4-nitrobenzene and 11.5 g of urea was ground in a mortar, after which the mixture was heated in a porcelain crucible in an oil bath at 200-205° for 1 hr. Here the liquid melt solidified with the evolution of ammonia. Then the crucible was cooled and the contents dissolved in 200 ml of dilute caustic solution, the solution boiled with carbon, the carbon removed by filtration, and the dark-red filtrate neutralized with acid. The obtained precipitate was filtered and then recrystallized from glacial acetic acid. We obtained 4.8 g of compound. Fine yellow-green needles, not melting at 325°.

Found %: C 52.48, 52.11; H 4.89, 4.82. $C_9H_9O_3N_3$. Calculated %: C 52.17; H 4.38.

4,7-Dimethyl-5-nitro-2-mercaptobenzimidazole. A mixture of 0.65 g of 1,2-diamino-3,6-dimethyl-4-nitrobenzene, 0.5 ml of carbon bisulfide, 10 ml of alcohol and 0.46 g of potassium hydroxide was heated in a flask fitted with reflux condenser for 3 hrs. Then the reaction mass was neutralized with acetic acid and evaporated in vacuo to dryness. The residue was reprecipitated from dilute alkali with acid, and then recrystallized from a large volume of alcohol. We obtained 0.3 g of substance as a dirty-yellow amorphous powder, not melting at 325°.

Found %: S 14.36, 14.50. $C_9H_9O_2N_3S$. Calculated %: S 14.36.

The amino derivatives were obtained by reducing the nitro products, as had already been described in a previous communication [1].

5-Amino-6-methylbenzimidazolone hydrochloride. For reaction we took 1 g of 5-methyl-6-nitrobenzimidazolone, 1.5 g of tin and 10 ml of concentrated hydrochloric acid. We obtained 0.8 g of the amine hydrochloride. Reprecipitation from water with hydrochloric acid gave the compound as coarse rhombic crystals, containing a molecule of water, and not having a sharp melting point.

Found %: C 44.21; H 5.72; N 19.44, 19.52. $C_8H_9ON_3 \cdot HCl \cdot H_2O$. Calculated %: C 44.14; H 6.02; N 19.31.

The picrate also does not have a good melting point and decomposes completely at 260°.

4,7-Dimethyl-5-aminobenzimidazolone hydrochloride. For reaction we took 2.8 g of the nitro derivative, 40 ml of concentrated hydrochloric acid and 5 g of tin. The hydrochloride of the amine crystallized from water as fine colorless needles. After two recrystallizations we obtained 2 g of substance, containing a molecule of crystallization water.

Found %: N 18.14, 18.39; Cl 15.71, 15.70. M 235, 229. $C_9H_{11}ON_3 \cdot HCl \cdot H_2O$. Calculated %: N 18.14; Cl 15.30. M 231.

5-Amino-4,7-dimethyl-6-(2,5-dichlorophenylazo)benzimidazolone. A solution of 0.25 g of 4,7-dimethyl-5-aminobenzimidazolone hydrochloride in 20 ml of water was treated with a solution of 0.4 g of the double salt of the diazo compound from 2,5-dichloroaniline with zinc chloride in 10 ml of water. After 15 min the precipitate was filtered, recrystallized from aqueous pyridine, then treated with boiling 4% acetic acid, and finally washed with water. Red powder, melting at 315°.

Found %: N 20.16, 20.04. $C_{15}H_{12}ON_5Cl_2$. Calculated %: N 20.00.

SUMMARY

5-Amino-6-methylbenzimidazolone is incapable of azo coupling, whereas 5-amino-4,7-dimethylbenzimidazolone reacts with diazo compounds to yield azo dyes. These observations support the validity of the earlier made conclusion that in the benzimidazolone molecule, under the influence of the nonaromatic imidazolone ring, the dual bonding of positions 5-6 is enhanced and the dual bonding of positions 4-5 and 6-7 is weakened.

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ORGANOMAGNESIUM SYNTHESIS AND PROPERTIES OF 1,1,1-TRIPHENYLALKYLMETHANES, 1,5-DIPHENYL-3-BENZYLPENTANE, AND 1-PHENYL-3-(2-PHENYLETHYL)TRIDECANE. II

M. A. Chel'tsova, A. D. Petrov, and Iu. P. Egorov

Earlier [1] we had described the synthesis of a number of triphenylalkylmethanes, obtained by the scheme: $(C_6H_5)_3CCl + RMgX \rightarrow (C_6H_5)_3CR$ and it showed that the melting (freezing) points decrease with increase in the length of the radical R, both for solid hydrocarbons of the triphenylalkylmethane series and for their liquid perhydrides, the tricyclohexylalkylmethanes. In the present investigation we continued the synthesis of these series of hydrocarbons up to $R=C_{10}H_{21}$, and it was found that in the triphenylalkylmethane series the minimum freezing point occurs at $R=C_7H_{15}$ (Table 3). With further increase in the chain length the melting (freezing) points of the hydrocarbons in this series begin to rise again. At the same time, in the $(C_6H_{11})_3CR$ series they continue to fall at both $R=C_9H_{19}$ and $R=C_{10}H_{21}$ (to be sure, these last two hydrocarbons congeal to a glass).

The UV-absorption spectra, obtained for both the normal triphenylalkylmethanes and the branched triphenylalkylmethanes with a methylene group located in either the β- or γ-position to the central carbon atom, proved to be similar. One of these spectra is shown in Fig. 1,b. When compared with the spectrum of triphenylmethane (Fig. 1, c) it becomes possible to discern their similarity, not only in the location of the band and its shape, but also in the close intensity. From these data it follows that the triphenylmethane group is a quite stable chromophore, and is not materially affected by the length and degree of branching of the hydrocarbon chain. This conclusion could have been expected, since a similar phenomenon also exists for other aromatic alkyl derivatives, for example, the alkylbenzenes and alkylnaphthalenes.

In contrast to the β- and γ-methyl derivatives and the triphenyl-n-alkylmethanes, the α-methyl derivative $(C_6H_5)_3C-\underset{\underset{C}{|}}{C}(C)_6$ possesses a UV-spectrum that differs in both the shape and intensity of the band (Fig. 1, a).

It is possible to assume that this difference is due to steric factors, as a result of which the CH_3 group disturbs the usual reaction of the aromatic rings through the C atom, i. e., it leads to some change in the electron levels of the system.

A second problem of our investigation was to study the effect of spreading the phenyl rings, i. e., of casting them from one carbon atom (which is the case, for example, with the 1,1,1-triphenylalkanes) to the terminal carbon atoms of the triphenylalkane chains (structures that are characterized by having the lowest freezing points), on the freezing points of triphenyl- and diphenylalkanes. For this we synthesized hydrocarbon (I) with composition $C_{24}H_{26}$, namely

$$C_6H_5CH_2COOC_2H_5 + 2BrMgCH_2CH_2C_6H_5 \rightarrow$$

$$\rightarrow C_6H_5CH_2CH_2\underset{\underset{CH_2C_6H_5}{|}}{C}OHCH_2CH_2C_6H_5 \xrightarrow[+H_2]{-H_2O} C_6H_5CH_2CH_2\underset{\underset{CH_2C_6H_5}{|}}{C}HCH_2CH_2C_6H_5$$

(I)

1,5-diphenyl-3-benzylpentane, which had the quite high m. p. of +55°, but which obviously was still approximately 50° lower than the m. p. of the isomeric hydrocarbon 1,1,1-triphenylhexane (the melting point of $C_{25}H_{24}$ is 153°, and that of $C_{25}H_{28}$ is +76°).

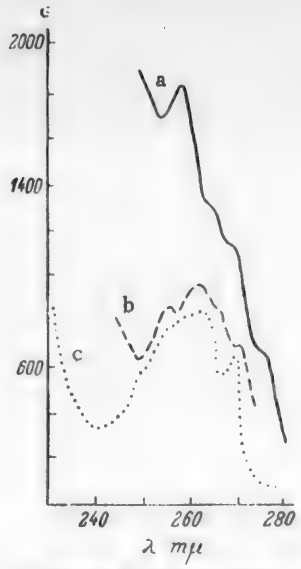

Fig. 1. UV-spectra of triphenylalkylmethanes in 2,2,4-trimethylpentane solution.

a – $(C_6H_5)_3C-C-C_8$, b – $(C_6H_5)_2CC_5H_{10}C-(C_6H_5)_2CH$.

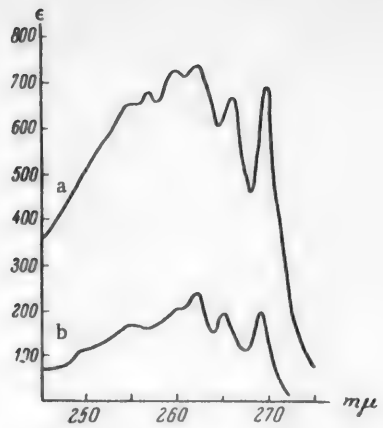

Fig. 2. UV-Spectrum of 1,5-diphenyl-3-benzylpentane. a) In 2,2,4-trimethylpentane solution, b) ethylbenzene.

The high freezing point of the indicated hydrocarbon, whereas its closest homolog (differing only by a CH_2 group) 1,5-diphenyl-3-(2-phenylethyl) pentane f. p. −32° [2], caused us at first to consider the possible cyclization of the olefin to the hydrindan derivative when it was hydrogenated under pressure. However, as the spectral study discussed below revealed, this derivative is absent.

Even in isooctane solution in the UV-spectra of the triphenylmethane compounds have a very diffuse character. The absorption bands almost do not have a fine structure. In this respect they differ from the monosubstituted aromatic compounds, in which this structure is well defined. The spectrum obtained for (I) shows a distinct fine structure, and in its shape and position of maxima the absorption band corresponds to that of a monosubstituted aromatic ring (Fig. 2).

Two UV-absorption curves are shown in Fig. 2: (a) is that of the investigated compound, and (b) is of ethylbenzene. In (a) we observe an approximately 3-fold increase in band intensity and the retention, as had already been indicated above, of a fine structure. This indicates that here we are dealing with three widely separated aromatic rings, in accordance with the postulated structure. The possible formation of an indan structure is indicated in the literature [3]; however, if we refer to the UV-spectrum of such a compound, it becomes possible to establish that the first maximum of its band is located at 273 mμ with an intensity of 1800 units. In our spectrum this portion shows an intensity of only 200 units, and any indication of an absorption band is completely lacking. Consequently, the formation of such a compound in noticeable amount must be rejected.

After all three rings had been hydrogenated, the resulting 1,5-dicyclohexyl-3-(cyclohexylmethyl) pentane had f. p. −20°. Tricyclohexylbutylmethane has f. p. +50° (crystals). Evidently, here also a spreading of the cyclohexyl rings made it possible to lower the freezing point by 50°. The effect of spreading the rings proved to be even more pronounced in the case of diphenylalkanes. Using the scheme given below, we synthesized hydrocarbon (II), 1-phenyl-3-(2-phenylethyl) tridecane ($C_{27}H_{40}$), which proved to have a freezing point of −60°. From the literature [4] it is known that 1,1-diphenyltetradecane ($C_{26}H_{38}$) has melting point +17.9°.

$$CH_2{=}CH(CH_2)_8COOC_2H_5 + 2C_6H_5CH_2CH_2MgBr \longrightarrow$$

$$\longrightarrow CH_2{=}CH(CH_2)_8C(CH_2CH_2C_6H_5)(OH)(CH_2CH_2C_6H_5) \xrightarrow[+2H_2]{-H_2O} C_6H_5CH_2CH_2CH(C_{10}H_{21})CH_2CH_2C_6H_5$$

(II)

TABLE 1

Physicochemical Properties of Triphenyl- and Diphenylalkanes

Formula	Boiling point (pressure in mm)	d_4^{40}	n_D^{40}	MR_D found	MR_D calc.	Empirical formula	Found (%) C	Found (%) H	Calculated (%) C	Calculated (%) H
$(C_6H_5)_3CC_7H_{15}$	220° (4)	1.0036	1.5730	112.3	111.5	$C_{26}H_{30}$	91.10	8.85	91.17	8.83
$(C_6H_5)_3CCH(CH_3)C_6H_{13}$	207—208 (3)	0.9960	1.5662	117.3	116.1	$C_{27}H_{32}$	90.44	9.00	90.94	9.01
$(C_6H_5)_3CC_9H_{19}$	189—190 (2)	0.9842	1.5620	121.75	120.76	$C_{28}H_{34}$	90.78	9.20	90.74	9.26
$(C_6H_5)_3CC_{10}H_{21}$	248—249 (3)	—	—	—	—	$C_{29}H_{36}$	90.35	9.55	90.56	9.45
$(C_6H_5CH_2CH_2)_2CHCH_2C_6H_5$	171—172 (1)	—	—	—	—	$C_{24}H_{26}$	90.60	9.62	91.66	8.34
$(C_6H_5CH_2CH_2)_2CHC_{10}H_{21}$	176—177 (1)	0.9154 (20°)	1.5169 (20°)	120.3	119.7	$C_{27}H_{40}$	89.36	10.66	88.94	11.06

TABLE 2

Physicochemical Properties of Tricyclohexyl- and Dicyclohexylalkanes

Formula	Boiling point (pressure in mm)	d_4^{40}	n_D^{40}	MR_D found	MR_D calc.	Empirical formula	Found (%) C	Found (%) H	Calculated (%) C	Calculated (%) H
$(C_6H_{11})_3CC_4H_9$	168—169 (0.5)	—	—	—	—	$C_{23}H_{42}$	86.97	12.95	86.68	13.32
$(C_6H_{11})_3CCH(CH_3)C_6H_{13}$	166—167 (0.5)	0.9269	1.5035	119.65	120.21	$C_{27}H_{50}$	86.74	13.07	86.51	13.49
$(C_6H_{11})_3CC_9H_{19}$	200—201 (3)	0.9167	1.4980	124.5	124.90	$C_{28}H_{52}$	86.65	13.40	86.49	13.51
$(C_6H_{11})_3CC_{10}H_{21}$	175—176 (1)	0.9119	1.4980	129.4	129.5	$C_{29}H_{54}$	86.35	13.24	86.46	13.54
$(C_6H_{11}CH_2CH_2)_2CHCH_2C_6H_{11}$	194—195 (1)	0.9035 *	1.4920 *	106.65	106.46	$C_{24}H_{44}$	86.62	13.29	86.66	13.34
$(C_6H_{11}CH_2CH_2)_2CHC_{10}H_{21}$	216—217 (1)	0.8995 *	1.4800 *	122.98	122.49	$C_{27}H_{52}$	86.45	13.65	86.08	13.92
$(C_6H_{11})_2CHC_9H_{19}$	146—147 (3)	0.8879 *	1.4820 *	99.57	99.40	$C_{22}H_{42}$	86.34	13.70	86.16	13.84
$(C_6H_{11})_2CHCH(CH_3)C_6H_{13}$	156—157 (4)	0.9090 *	1.4960 *	93.82	94.78	$C_{21}H_{40}$	86.40	13.57	86.08	13.92

* At 20°.

The melting points and viscosities of the triphenyl-, diphenyl-, tricyclohexyl- and dicyclohexylalkanes that we synthesized in the present study are given in Table 3. Other physical properties of these hydrocarbons and their elemental analysis data are given in Tables 1 and 2.

EXPERIMENTAL*

The triphenylchloromethane taken for reaction was purified to constant melting point by repeated recrystallization, and the bromides were purified by 2-3 distillations through a column having an efficiency of 20 theoretical plates at 20-40 mm. The yields of the hydrocarbons ranged from approximately 20 to 30%. About 100-150 g of each hydrocarbon was prepared. To effect complete hydrogenation the triphenylalkanes were hydrogenated under pressure over Raney-Ni at 150-170°. 1,1-Dicyclohexyl-2-methyloctane and 1,1-dicyclohexyldecane were isolated in the hydrogenation of 1,1,1-triphenyl-2-methyloctane and 1,1,1-triphenyldecane, being obtained as the result of one ring cleaving from the starting hydrocarbons during hydrogenation.

TABLE 3

Melting Points and Viscosities of Triphenyl-, Diphenyl-, Tricyclohexyl- and Dicyclohexylalkanes

Formula	Melting (freezing) point	Viscosity (in centistokes)				
		0°	20°	50°	100°	150°
$(C_6H_5)_3CC_7H_{15}$	+ 15 gl.	—	—	572.0	15.0	3.7
$(C_6H_5)_3CCHC_6H_{13}$ (CH$_3$)	+ 15 gl.	—	—	422.0	15.8	4.9
$(C_6H_5)_3CC_9H_{19}$	30 cryst.	—	—	91.0	8.2	2.9
$(C_6H_5)_3CC_{10}H_{21}$	42 cryst.	—	—	92.0	10.6	3.3
$(C_6H_5CH_2CH_2)_2CHCH_2C_6H_5$	55 cryst.	—	—	—	—	—
$(C_6H_5CH_2CH_2)_2CHC_{10}H_{21}$	—60 gl.	—	12.1	4.4	—	—
$(C_6H_{11})_3CC_4H_9$	50 cryst.	—	—	—	—	—
$(C_6H_{11})_3CC_4H_9$-iso	47 cryst.	—	—	—	—	—
$(C_6H_{11})_3CC_6H_{13}$	+ 10 gl.	—	—	635.0	19.4	3.2
$(C_6H_{11})_3CCHC_6H_{13}$ (CH$_3$)	+ 2 gl.	—	—	431.0	16.5	4.0
$(C_6H_{11})_3C_9H_{19}$	+ 3 gl.	—	—	133.6	8.2	4.4
$(C_6H_{11})_3CC_{10}H_{21}$	— 5 gl.	—	—	130.0	12.1	3.4
$(C_6H_{11}CH_2CH_2)_2CHCH_2C_6H_{11}$	—20 gl.	—	501.5	48.4	7.0	2.4
$(C_6H_{11}CH_2CH_2)_2CHC_{10}H_{21}$	—50 gl.	170.9	47.5	18.3	14.5	2.07
$(C_6H_{11})_2CHC_9H_{19}$	—10 gl.	169.3	44.9	10.8	2.6	1.4

1,5-Diphenyl-3-benzylpentane. Here 1-bromo-2-phenylethane, one of the starting products, was obtained by us in 90% yield using the method of [5], i. e., by the slow distillation of 2-phenylethanol with 48% HBr. B. p. 105° (18 mm), $n^{20}D$ 1.5570, d^{20}_4 1.3643. From [6], b. p. 99° (15 mm), $n^{20}D$ 1.5572 (yield 92%). We obtained 350 g of phenylacetic acid (m. p. 74-75°) from 750 g of benzyl chloride, from which we prepared 170 g of the ethyl ester with b. p. 188° (11 mm), $n^{20}D$ 1.5020, d^{20}_4 1.0314. From [7], b. p. 227.1° (760 mm), $n^{18.5}D$ 1.4992, d^{20}_4 1.0333. From 170 g of ethyl phenylacetate and $C_6H_5CH_2CH_2MgBr$ (from 430 g of $C_6H_5CH_2CH_2Br$) we obtained 88 g (30%) of 1,5-diphenyl-3-benzyl-3-pentanol.

B. p. 263° (5 mm), 225° (1 mm), $n^{20}D$ 1.5855, d^{20}_4 1.0658, MR_D 103.90; calculated 103.75. Found %: C 87.77; H 7.94; OH 5.4. $C_{24}H_{26}O$. Calculated %: C 87.22; H 7.94; OH 4.0.

We used the procedure of [8] to dehydrate 1,5-diphenyl-3-benzyl-3-pentanol. A mixture of 88 g of the carbinol, 140 g of glacial acetic acid and 1 ml of conc. H_2SO_4 was heated on the water bath for 30 min, after which the unsaturated hydrocarbon was isolated in conventional manner.

B. p. 206-207° (2 mm), d^{20}_4 1.0307, $n^{20}D$ 1.5890 (yield 53%), MR_D 102.93; calculated 101.76. Found %: C 92.18; H 7.87. $C_{24}H_{24}$. Calculated %: C 92.25; H 7.75.

* V. P. Krukhtanova and I. N. Lifanova assisted in the experimental portion of this investigation.

An exaltation of 1.17 units makes it possible to assume that the hydrocarbon has the structure of (III).

$$C_6H_5CH_2CH_2CCH_2CH_2C_6H_5$$
$$\|$$
$$CHC_6H_5$$
(III)

The hydrocarbon (22 g) was first hydrogenated under pressure at 100-120° over Bag catalyst [9]. Here a product with m. p. 55° was obtained. To effect complete hydrogenation, 22 g of the unsaturated hydrocarbon was hydrogenated under pressure at 150-170° over Raney-Ni. The naphthenic hydrocarbon obtained here had f. p. −20°.

1-Phenyl-3-(2-phenylethyl) tridecane. 1-Phenyl-3-(2-phenylethyl)-12-tridecen-3-ol was obtained in 82% yield from $C_6H_5CH_2CH_2MgBr$ (from 215 g of $C_6H_5CH_2CH_2Br$) and 122 g of ethyl undecylenate.

B. p. 263° (4 mm), d^{20}_4 0.9585, $n^{20}D$ 1.5315, MR_D 122.2, calculated 122.8. Found %: C 86.33; H 10.19; OH 4.48. $C_{27}H_{36}O$. Calculated %: C 86.65; H 10.12; OH 4.49.

The compound was dehydrated in the same manner as indicated above for 1,5-diphenyl-3-benzyl-3-pentanol. We obtained 107 g (60%) of mixed dienic hydrocarbons from 178 g of the carbinol.

B. p. 195 (1 mm), d^{20}_4 0.9364, $n^{20}D$ 1.5307. MR_D 119.05; calculated 118.75. Found %: C 89.72; H 10.10. $C_{27}H_{36}$. Calculated %: C 89.92; H 10.08.

45 g of the dienic hydrocarbon mixture was hydrogenated under pressure at 100° over Bag catalyst. We obtained 36 g of hydrogenated product. The hydrocarbon had f. p. −60° (its structurally similar 1-phenyl-3-(2-phenylethyl) undecane freezes at −54° and has d^{20}_4 0.9215 and $n^{20}D$ 1.5192). 30 g of the mixed dienic hydrocarbons was hydrogenated under pressure at 150-170° over Raney-Ni. We obtained 24 g (91.7%) of 1-phenyl-3-(2-phenylethyl)-tridecane.

SUMMARY

1. Fourteen new hydrocarbons were synthesized [1,1,1-triphenyloctane, 1,1,1-triphenyl-2-methyloctane, 1,1,1-triphenyldecane, 1,1,1-triphenylundecane, 1,5-diphenyl-3-benzylpentane, 1-phenyl-3-(2-phenylethyl) tridecane, 1,1,1-tricyclohexylpentane, 1,1,1-tricyclohexyl-2-methyloctane, 1,1,1-tricyclohexyldecane, 1,1,1-tricyclohexylundecane, 1,1-dicyclohexyl-2-methyloctane, 1,1-dicyclohexyldecane, 1,5-dicyclohexyl-3-(cyclohexylmethyl) pentane and 1-cyclohexyl-3-(2-cyclohexylethyl) tridecane, and their melting (freezing) points and viscosities were determined.

2. It was shown that in the triphenylalkylmethane series both the viscosity and freezing point decrease with increase in the length of the alkyl chain up to C_7H_{15}, after which they begin to increase again. Apparently, a similar minimum also exists in the tricyclohexylalkylmethane series, but here it could not be fixed due to the fact that both the tricyclohexylnonyl- and -decylmethanes congeal to a glass.

3. It was found that transition from 1,1,1-tricyclohexylpentane to 1,5-dicyclohexyl-3-(cyclohexylmethyl) pentane and from 1,1-diphenyltetradecane to 1-phenyl-3-(2-phenylethyl) tridecane results in substantial decrease in the freezing points, being caused by a spreading of the cyclohexyl (phenyl) rings in the hydrocarbon molecules.

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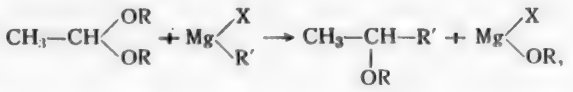
REACTION OF EXCHANGE OF HYDROXYL GROUPS FOR RADICALS OF ORGANOMAGNESIUM COMPOUNDS

II. REACTION OF GRIGNARD REAGENT WITH SYMMETRIC ACETALS

M. F. Shostakovskii and M. R. Kulibekov

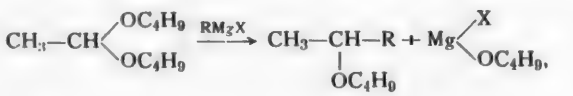
In the previous paper [1] we studied the reactivity of mixed acetals when reacted with Grignard reagent and established that here it is the heavier hydroxy radical of the mixed acetal that exchanges for the radical of the organomagnesium compound. At the same time it was shown that the alkyl aryl acetals are highly reactive in this sense.

As a continuation of this study, we set out to investigate the reaction of Grignard reagent with symmetric acetals of the aliphatic, aliphatic-aromatic and aromatic series, and to develop methods for the synthesis of the corresponding ethers, some of them being difficultly accessible. In addition, it was of interest to study the specific influence exerted by different radicals in the Grignard reagent on the exchange reaction with symmetric acetals. As regards the reactivity of symmetric acetals, then on the basis of experimental data it is possible for us to state that in contrast to the mixed acetals they show a number of peculiarities, associated with the fact that both of the hydroxy radicals are the same. This creates a certain equilibrium in the molecule, which when disturbed results in exchange proceeding very smoothly by the scheme



where R = Alk, Ar or aralkyl radical.

Although a number of statements exist in the literature [2] on the exchange of alkoxyl groups by radicals of organomagnesium compounds, still they all fail to touch upon the problems associated with the course of the exchange reaction. For study we took three groups of symmetric acetals, namely the dialkyl, diaryl and sym. diaralkyl acetals. The dialkyl acetals taken for study were the dibutyl and diethyl acetals. When dibutyl acetal was reacted with butylmagnesium bromide, isoamylmagnesium bromide, benzylmagnesium chloride and phenylmagnesium bromide, in all cases one of the butoxy groups was replaced by the indicated radicals of the Grignard reagent to yield the corresponding ether



where: R = n-C_4H_9, iso-C_5H_{11}, $CH_2C_6H_5$ or C_6H_5.

When dibenzyl acetal was reacted with isoamylmagnesium bromide, benzylmagnesium chloride and phenylmagnesium bromide, it was found that in contrast to the dialkyl acetals the exchange reaction proceeds with somewhat greater difficulty, i. e., drastic reaction conditions are required, which we were able to achieve by running the reaction without solvent at elevated temperature (110-120°). Under these conditions one of the benzyloxy

groups is replaced by radicals of the Grignard reagent to yield the corresponding ethers. When diphenyl acetal is reacted with butylmagnesium bromide the exchange reaction proceeds with great vigor to yield the corresponding phenyl ether of 2-hexanol. For this reason the reaction was run under milder conditions than before, i. e., it was run by adding the diphenyl acetal to an ether solution of the organomagnesium compound. Based on the experimental data, we established that the ability of hydroxy radicals to exchange decreases in the order: OC_6H_5 > > OAlk > $OCH_2C_6H_5$. Some of the constants of the ethers synthesized by us are given in the table.

EXPERIMENTAL

1. Reaction of dibutyl acetal with isoamylmagnesium bromide. 30 g of dibutyl acetal with b. p. 184.5° (747 mm), d^{20}_4 0.8257, $n^{20}D$ 1.4074, heated in a boiling water bath, was treated with an ether solution of isoamylmagnesium bromide, prepared from 8 g of magnesium and 50 g of isoamyl bromide. In order to raise the temperature of the reaction mixture the diethyl ether was distilled off as fast as it was added to the reaction flask. Heating was continued for about 2 hrs after all of the organomagnesium compound had been added. When all of the diethyl ether had been distilled off, the product developed intense self-heating (frothing) inside the reaction flask. The reaction product was decomposed with water, acidulated with acetic acid. If unreacted organomagnesium was absent, the decomposition with water went slowly with very little heat evolution. After decomposition, the oily product was separated from the water layer, washed with 10% HCl solution to hydrolyze any unreacted acetal, and then taken up in ether. The ether solution was washed with water, then with dilute soda solution, again with water, and finally it was dried over anhydrous sodium sulfate. The ether was distilled off on the water bath. The residue was distilled at atmospheric pressure; the following fractions were obtained at a pressure of 735 mm:

1st fraction, b. p. 74-158° (several drops); 2nd fraction, b. p. 159-175°, 1.5 g; 3rd fraction , b. p. 176-182°, 12 g; 4th fraction, b. p. 183-184°, 3 g.

The 4th fraction was unreacted acetal. The 3rd fraction was redistilled; here we obtained 10 g (50.8%) of the butyl ether of 2-methyl-5-hexanol, being a mobile, colorless, clear liquid with a fruity odor, insoluble in water, and readily soluble in organic solvents. Three other ethers were synthesized in a similar manner. The constants of all of the synthesized ethers are given in the table.

2. Reaction of diethyl acetal with phenylmagnesium bromide. Under the conditions of Expt. 1 we added the phenylmagnesium bromide, obtained from 3 g of magnesium and 19 g of bromobenzene, to 15 g of diethyl acetal. The reaction product was vacuum-distilled (12 mm). The following fractions were obtained: 1st fraction, b. p. 45-72°, 1.5 g; 2nd fraction, 73-82°, 9.5 g; residue 1.5 g.

Redistillation of the 2nd fraction from sodium gave 7 g (57.3%) of a liquid with b. p. 81-82° (13 mm), $n^{20}D$ 1.4905, d^{20}_{20} 0.9282. This product corresponds to the ethyl ether of 1-phenylethyl alcohol, which, according to the literature [1], has b. p. 185-187° and $d^{21.5}$ 0.931.

3. Reaction of dibenzyl acetal with isoamylmagnesium bromide. To the isoamylmagnesium bromide, obtained from 3 g of magnesium and 18 g of isoamyl bromide, heated after removal of the ether to 110°, was added 12 g of dibenzyl acetal. After mixing, the reactant mixture was heated for 1.5 hrs at 120°. The product was isolated in conventional manner and then vacuum-distilled. Redistillation from sodium metal gave 5 g (50%) of the benzyl ether of 2-methyl-5-hexanol. It was obtained as a colorless clear liquid with aromatic odor, insoluble in water, and readily soluble in organic solvents.

B. p. 129-131° (15 mm), $n^{20}D$ 1.4790, d^{20}_4 0.9001, MR_D 64.90; calculated 64.89. Found %: C 81.48, 81.30; H 10.61, 10.61. $C_{14}H_{22}O$. Calculated %: C 81.55; H 10.67.

The dibenzyl acetal for the given synthesis was obtained by us for the first time in good yield by heating butyl benzyl acetal in the presence of hydrochloric acid.

B. p. 184.5-185° (13 mm), $n^{20}D$ 1.5394, d^{20}_4 1.0500. MR_D 72.25; calculated 72.17. Found %: C 79.07, 78.89; H 7.51, 7.55. $C_{15}H_{18}O_2$. Calculated %: C 79.33; H 7.44.

Dibenzyl acetal is a colorless, clear, oily liquid with a slight odor. It is insoluble in water, and readily soluble in organic solvents. Two other ethers were synthesized by us under the above given conditions (see table).

4. Reaction of diphenyl acetal with butylmagnesium bromide. In constrast to the previous experiments this reaction was run in ether medium. To the butylmagnesium bromide, obtained from 3 g of magnesium and

Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	Found (%) H	Calc. (%) C	Calc. (%) H	Literature data
$CH_3-CH(OC_2H_5)(C_6H_5)$	81—82 (13)	1.4905	0.9282	—	—	— —	— —	—	—	B. p. 185—187°, $d^{21.9}$ 0.931 [1]
$CH_3-CH(OC_4H_9\text{-n})(C_4H_9\text{-n})$	169—171 (740)	1.4096	0.7883	50.06	50.02	76.73, 76.68	14.00, 14.08	76.94	13.92	
$CH_3-CH(OC_4H_9\text{-n})(C_5H_{11}\text{-iso})$	176—178 (735)	1.4133	0.7817	54.89	54.64	77.02, 76.81	13.95, 14.05	76.74	13.95	
$CH_3-CH(OC_4H_9\text{-n})(CH_2C_6H_5)$	132—134 (20)	1.4897	0.9109	60.87	60.55	81.74, 81.64	10.20, 10.10	81.25	10.41	
$CH_3-CH(OC_4H_9\text{-n})(C_6H_5)$	119—120 (14)	1.4840	0.9100	—	—	— —	— —	—	—	B. p. 220—225° (730), d_4^{20} 0.9063, n_D^{20} 1.4832 [3]
$CH_3-CH(OCH_2C_6H_5)(C_5H_{11}\text{-iso})$	129—131 (15)	1.4790	0.9001	64.90	64.89	81.48, 81.30	10.61, 10.61	81.55	10.67	
$CH_3-CH(OCH_2C_6H_5)(CH_2C_6H_5)$	178—179 (14)	1.5430	1.0365	69.52	68.76	83.45, 83.66	7.73, 7.75	84.09	7.96	
$CH_3-CH(OCH_2C_6H_5)(C_6H_5)$	175—177 (20)	1.5552	1.0249	66.40	65.91	83.93, 83.77	7.59, 7.55	83.90	7.54	
$CH_3-CH(OC_6H_5)(C_4H_9\text{-n})$	129—132 (29)	1.4964	0.9304	55.93	55.66	80.91, 80.28	9.76, 9.82	80.80	10.11	

17 g of butyl bromide, without distilling off the ether, was added 10 g of the acetal, and the whole heated on the water bath. Here the reaction mixture showed strong frothing and changed completely to a white solid mass. After decomposition, the product was isolated and vacuum-distilled (15 mm). The following fractions were obtained: 1st fraction, b. p. 82-86°, 3 g; 2nd fraction, b. p. 87-116°, 2.5 g; 3rd fraction, 117-137°, 4.5 g.

The 1st and 2nd fractions reacted with sodium and had a phenolic odor. The 3rd fraction, reacting weakly with sodium, was redistilled to give the phenyl ether of 2-hexanol. Clear colorless liquid with a slight odor. Insoluble in water, and readily soluble in organic solvents.

B. p. 129-132° (29 mm), $n^{20}D$ 1.4964, d^{20}_4 0.9304, MR_D 55.93; calculated 55.66. Found %: C 80.91, 80.28; H 9.76, 9.82. $C_{12}H_{18}O$. Calculated %: C 80.80; H 10.11.

SUMMARY

1. A study was made of the reaction for the exchange of the hydroxy radicals of symmetric acetals by radicals of the Grignard reagent.

2. The behavior of different hydroxy radicals in the exchange reaction was shown. It was found that the phenoxy group enters easiest into the exchange reaction, and that aralkoxy radicals exchange with the greatest difficulty. Alkoxy groups occupy a middle position.

3. Synthesized for the first time were the butyl ethers of 2-methyl-5-hexanol, 2-phenylpropyl alcohol and 1-phenylethyl alcohol, the benzyl ethers of 2-phenylpropyl alcohol and 1-phenylethyl alcohol, the phenyl ether of 2-hexanol, and dibenzyl acetal.

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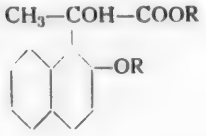
STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XVIII. SYNTHESIS OF ESTERS OF α-(β-ALKOXY-1-NAPHTHYL) LACTIC ACIDS

I. I. Lapkin and V. Ia. Vlasova

In studying the reactions of esters of α-keto acids with mixed organomagnesium compounds it was found by Grignard [1] that when the reactants are taken in equivalent proportions it is the more active keto group that reacts, and only when the Grignard reagent is taken in excess does the ester group react. Later studies added some modifications to this general rule. It was established by one of us [2] that esters of organic acids weaker than oxalic acid either do not react or react only slightly with arylmagnesium halides that contain alkyl radicals in the ortho-position. Later it was shown [3] that the ester group found in esters of α-keto acids, being acids weaker than oxalic acid, does not react with di-o-substituted arylmagnesium halides, and even with a large excess of the Grignard reagent only the keto group reacts, as a consequence of which the esters of tertiary α-hydroxy acids are the solitary reaction product. This method was used to synthesize such interesting and broadly important compounds as the esters of α-(β-alkoxy-1-naphthyl) lactic acids.

As is known, the naphthalene ring shows a number of properties that differentiate it from the benzene ring. Of these properties it is most important to mention the high reactivity shown by the carbon atom in the α-position. Together with this, the second ring in naphthalene is stereochemically almost equivalent to one ortho-substituent, attached to the benzene ring and creating steric hindrance. A system also stereochemically almost equivalent to a benzene ring with two ortho-substituents is obtained when an alkoxyl group is present in the β-position of the naphthalene ring. For this reason organomagnesium compounds, obtained from α-bromo-β-methoxy- and α-bromo-β-ethoxynaphthalene, react with the esters of pyruvic acid in exactly the same manner as the di-o-substituted arylmagnesium halides, i. e., with the formation of esters of α-(β-methoxy-1-naphthyl)- and α-(β-ethoxy-1-naphthyl) lactic acids of general formula (I).



(I)

The activity of the α-carbon atom in the naphthalene ring is reflected in a comparatively greater yield of reaction products. Our experimental results are given in the table.

EXPERIMENTAL

Reaction between the esters of pyruvic acid and the organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, was accomplished using the conventional conditions for Grignard reactions. Since the bromides proved to be comparatively insoluble in anhydrous ether we used a 50-50 volume mixture of toluene and ether, as the solvent. As had already been indicated, organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, are stereochemically similar to di-o-substituted arylmagnesium halides, for which reason the order of mixing the reactants is not important. In all of the experiments the starting compounds were taken in $^1/_8$ mole amounts. The time of heating the reaction mixture was 2 hrs. The Grignard complex was decomposed with 10% acetic acid. After solvent removal by distillation the product was purified by vacuum-distillation,

Reactants (1 : 1)	Formula of ester*	Yield (in %)	Boiling point (pressure in mm)	Melting point	Empirical formula	Content (in %)							
						C		H		OH		OR	
						found	calc.	found	calc.	found	calc.	found	calc.
2-Methoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(2-methoxy-1-naphthyl) lactate	35	182—184° (5)	110°	$C_{15}H_{16}O_4$	69.14	69.21	6.39	6.20	5.8	6.5	21.8	23.8
2-Methoxy-1-naphthylmagnesium bromide + ethyl pyruvate	Ethyl α-(2-methoxy-1-naphthyl) lactate	58	186—188 (5)	107	$C_{16}H_{18}O_4$	69.99	70.05	6.72	6.61	5.5	6.2	—	—
2-Methoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(2-methoxy-1-naphthyl) lactate	63	200—202 (4)	61—62	$C_{18}H_{22}O_4$	71.25	71.50	7.16	7.32	5.3	5.6	—	—
2-Methoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(2-methoxy-1-naphthyl) lactate	57	201—203 (5)	66—67	$C_{18}H_{22}O_4$	71.63	71.50	7.24	7.32	5.2	5.6	—	—
2-Ethoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(2-ethoxy-1-naphthyl) lactate	32	208—210 (10)	131—132	$C_{16}H_{18}O_4$	69.78	70.05	6.48	6.61	6.0	6.2	—	—
2-Ethoxy-1-naphthylmagnesium bromide + ethyl pyruvate	Ethoxy α-(2-ethoxy-1-naphthyl) lactate	50	203—205 (5)	90—91	$C_{17}H_{20}O_4$	70.53	70.81	6.90	6.99	5.1	5.9	27.6	31.2
2-Ethoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(2-ethoxy-1-naphthyl) lactate	61	207—209 (5)	33—34	$C_{19}H_{24}O_4$	72.26	72.12	7.56	7.65	5.0	5.4	—	—
2-Ethoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(2-ethoxy-1-naphthyl) lactate	55	199—201 (4)	61—62	$C_{19}H_{24}O_4$	71.91	72.12	7.71	7.65	5.3	5.4	—	—

followed by recrystallization from a mixture of petroleum ether and toluene (2:1). That reaction was normal was evidenced by the fact that all of the synthesized esters of α-(2-methoxy-1-naphthyl) lactic acid when saponified with 5% alcoholic KOH solution are converted to the same α-(2-methoxy-1-naphthyl) lactic acid. M. p. 155° (from aqueous alcohol). Not described in the literature.

Found %: C 68.09; H 5.52; OH 13.2; OCH_3 11.1. $C_{14}H_{14}O_4$. Calculated %: C 68.28; H 5.73; OH 13.8; OCH_3 12.6.

Saponification of the esters of α-(2-ethoxy-1-naphthyl) lactic acid gave α-(2-ethoxy-1-naphthyl) lactic acid, which after recrystallization from aqueous alcohol had m. p. 184-185° (with decomp.). This acid is also new in the literature.

Found %: C 69.05; H 6.11; OH 12.0; OC_2H_5 15.9. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.20; OH 13.1; OC_2H_5 17.3.

SUMMARY

It was established that the mixed organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, being stereochemically similar to di-o-substituted arylmagnesium halides, react in a similar manner with esters of pyruvic acid, i. e., only with the keto group, and not with the ester group, and it was also established that the formation of esters of α-(2-alkoxy-1-naphthyl) lactic acids is the final step in the indicated reaction.

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Perm State University

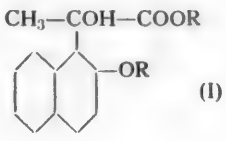
STERIC HINDRANCE IN ORGANOMAGNESIUM REACTIONS

XIX. SYNTHESIS OF ESTERS OF α-(4-ALKOXY-1-NAPHTHYL) LACTIC ACID

I. I. Lapkin and O. M. Lapkina

In previous communications [1, 2] we had shown that when esters of α-keto acids, the latter being comparatively weak acids (in comparison to oxalic acid [3]), are reacted with di-ortho-substituted arylmagnesium halides, it is only the keto group that reacts; even with a large excess of the organomagnesium compound the ester group is not reactive here. It was also shown that the mixed organomagnesium compounds, obtained from α-bromo-β-alkoxynaphthalenes, stereochemically being compounds almost equivalent to di-ortho-substituted arylmagnesium halides, react only with the keto group. The organomagnesium compounds, obtained from 1-bromo-4-alkoxynaphthalenes, are stereochemically analogous to mono-ortho-substituted arylmagnesium halides, and for this reason behave in a similar manner [1] when reacted with esters of α-keto acids (pyruvic acid), i. e., they also react only with the more active keto group.

This circumstance can be utilized to conveniently synthesize the esters of α-(4-alkoxy-1-naphthyl) lactic acids of general formula (I). This is supported by the experimental results summarized in the table.



(I)

EXPERIMENTAL

The following conditions were used to react the esters of pyruvic acid with the mixed organomagnesium compounds, obtained from 1-bromo-4-alkoxynaphthalenes. To the activated magnesium, contained in a flask and covered with anhydrous ether, was added the bromide, dissolved in three volumes of ether. The bromide was taken in $^1/_7$ mole amount in all of the experiments. The pyruvic ester, dissolved in an equal volume of ether, was then slowly added to the prepared organomagnesium compound, and here a copious yellow precipitate usually formed in the flask. The mixture was heated for 2 hrs, and then decomposed in conventional manner with water and 10% acetic acid. The ether layer was separated from the aqueous layer, washed with water, then with 10% soda solution, and again with water until neutral. After removal of the solvent by distillation, the product was vacuum-distilled, purified to constant melting point by recrystallization from a mixture of toluene and petroleum ether, and analyzed.

All of the synthesized esters of α-(4-alkoxy-1-naphthyl) lactic acids were saponified with 5% alcoholic KOH solution. Saponification of the esters of α-(4-methoxy-1-naphthyl) lactic acid gave α-(4-methoxy-1-naphthyl) lactic acid. M. p. 130-132° (from toluene).

Found %: C 68.40; H 5.68; OH 13.6; OCH_3 10.8. $C_{14}H_{14}O_4$. Calculated %: C 68.28; H 5.73; OH 13.8; OCH_3 12.6.

Recrystallization of the acid from either water or 30% alcohol gave the hydrate of this acid. M. p. 102-103°.

Reactants (1 : 1)	Formula of ester*	Yield (in %)	Boiling point (pressure in mm)	Melting point	Empirical formula	Content (%)							
						C		H		OH		OR	
						found	calc.	found	calc.	found	calc.	found	calc.
4-Methoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(4-methoxy-1-naphthyl) lactate	38	187—189° (6)	117—118°	$C_{15}H_{16}O_4$	68.97	69.21	6.11	6.20	6.2	6.5	21.1	23.8
4-Methoxy-1-naphthylmagnesium bromide + ethyl pyruvate	Ethyl α-(4-methoxy-1-naphthyl) lactate	60	191—193 (6)	75—76	$C_{16}H_{18}O_4$	69.83	70.05	6.60	6.61	5.6	6.2	—	—
4-Methoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(4-methoxy-1-naphthyl) lactate	56	212—214 (7)	72—73	$C_{18}H_{22}O_4$	71.21	71.60	7.31	7.32	5.2	5.6	—	—
4-Methoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(4-methoxy-1-naphthyl) lactate	45	205—207 (6)	73—74	$C_{18}H_{22}O_4$	71.32	71.50	7.22	7.32	5.3	5.6	—	—
4-Ethoxy-1-naphthylmagnesium bromide + methyl pyruvate	Methyl α-(4-ethoxy-1-naphthyl) lactate	36	191—193 (6)	119—120	$C_{16}H_{18}O_4$	69.90	70.05	6.83	6.61	5.9	6.2	—	—
4-Ethoxy-1-naphthylmagnesium bromide + ethyl pyrivate	Ethyl α-(4-ethoxy-1-naphthyl) lactate	58	188—190 (4)	80—81	$C_{17}H_{20}O_4$	70.61	70.81	7.02	6.99	5.6	5.9	27.1	31.2
4-Ethoxy-1-naphthylmagnesium bromide + n-butyl pyruvate	n-Butyl α-(4-ethoxy-1-naphthyl) lactate	54	212—214 (6)	64—65	$C_{19}H_{24}O_4$	71.85	72.12	7.59	7.65	5.1	5.4	—	—
4-Ethoxy-1-naphthylmagnesium bromide + isobutyl pyruvate	Isobutyl α-(4-ethoxy-1-naphthyl) lactate	40	191—193 (3)	103—104	$C_{19}H_{24}O_4$	72.15	72.12	7.45	7.65	5.2	5.4	—	—

Found %: C 63.44; H 6.02. $C_{14}H_{14}O_4 \cdot H_2O$. Calculated %: C 63.63; H 6.11.

Saponification of the esters of α-(4-ethoxy-1-naphthyl) lactic acid gave α-(4-ethoxy-1-naphthyl) lactic acid. M. p. 168-170° (from toluene).

Found %: C 69.00; H 6.08; OH 11.8; OC_2H_5 15.3. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.20; OH 13.1; OC_2H_5 17.3.

Recrystallization from either water or 30% alcohol gave the hydrate of this acid. M. p. 101-102°.

Found %: C 64.52; H 6.41. $C_{15}H_{16}O_4 \cdot H_2O$. Calculated %: C 64.73; H 6.52.

Both of the above acids are new in the literature.

The esters of pyruvic acid, used in the reactions, were obtained by heating pyruvic acid with an excess of the anhydrous alcohols, followed by the slow removal by distillation of the formed water and excess alcohol. Methyl pyruvate, b. p. 135-136°. Ethyl pyruvate, b. p. 54° (18 mm). Butyl pyruvate:*

B. p. 69° (12 mm), $d^{18.5}_4$ 0.9926, $n^{18.5}D$ 1.4165, MR_D 36.49; calculated 36.19. Found %: C 58.13; H 8.30. $C_7H_{12}O_3$. Calculated %: C 58.31; H 8.39.

Isobutyl pyruvate:*

B. p. 67° (14 mm), $d^{18.5}_4$ 0.9873, $n^{18.5}D$ 1.4131, MR_D 36.42; calculated 36.19. Found %: C 58.15; H 8.32. $C_7H_{12}O_3$. Calculated %: C 58.31; H 8.39.

SUMMARY

It was established that the method of preparing esters of α-aklyl- and arylIactic acids by reacting organomagnesium compounds with esters of pyruvic acid is entirely suitable for the synthesis of esters of α-(4-alkoxy-1-naphthyl) lactic acids.

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Perm State University

* New compound.

** Original Russian pagination. See C. B. translation.

HETEROCYCLIC COMPOUNDS

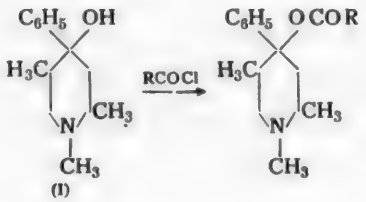
61. SYNTHETIC ANALGESIC SUBSTANCES

XXV. ESTERS OF 1,2,5-TRIMETHYL-4-PHENYL(ARYL)-4-PIPERIDOL

I. N. Nazarov,* N. S. Prostakov, and N. N. Mikheeva

In previous communications [1] we had described the synthesis of various esters of 1,2,5-trimethyl-4-phenyl-(aryl)-4-piperidols, and had shown that the character of the physiological action of these compounds depends to a large degree on the nature of the acyl radical. The esters of the aliphatic acids are usually analgesics, whereas the esters of the aromatic and aliphatic-aromatic acids prove to be local anesthetics.

To study the influence of the structure of esters of 1,2,5-trimethyl-4-phenyl-4-piperidols on their physiological activity we synthesized a new series of compounds of this type. Using the acid chlorides we esterified the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m. p. 107-108°) (I), the propionic ester of which is a powerful analgesic, widely used at the present time under the name of "promedol" [2].



(I)

In this manner we prepared the p-methoxyphenoxyacetic (II), p-ethoxyphenoxyacetic (III), α-phenoxypropionic (IV), α-phenoxyisobutyric (V), α-p-chlorophenoxyisobutyric (VI), p-nitrophenoxyacetic (VII), p-aminophenoxyacetic (VIII), diphenylacetic (IX), phenylpropiolic (X), pyromucic (XI) and β-phenylmercaptopropionic (XII) esters of the γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol.

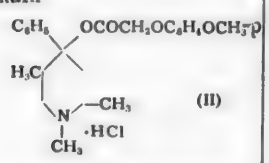
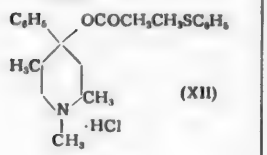
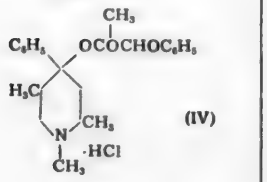
Based on the data of the pharmacological testing, made in the M. I. Mashkovskii laboratory, some of the indicated esters show appreciable local anesthetic action. Especially outstanding are the β-phenylmercaptopropionic (XII) and p-methoxyphenoxyacetic (II) esters, which are much more powerful than dikain** and at the same time are appreciably less toxic. The anesthetic activity of esters (II) and (XII) does not change after sterilization. The phenylpropiolic ester (X) proves to be a strong irritant. The degree of anesthetic activity, determined by the Regnier method, of some of the compounds prepared by us is shown in the table.

The chloride of β-phenylmercaptopropionic acid, used to synthesize ester (XII), was obtained from thiophenol and acrylonitrile in 75% yield by the scheme

$$C_6H_5SH + CH_2{=}CH{-}CN \longrightarrow C_6H_5SCH_2CH_2CN \xrightarrow[HCl]{H_2O}$$
$$\longrightarrow C_6H_5SCH_2CH_2COOH \xrightarrow{SOCl_2} C_6H_5SCH_2CH_2COCl.$$

* Deceased.

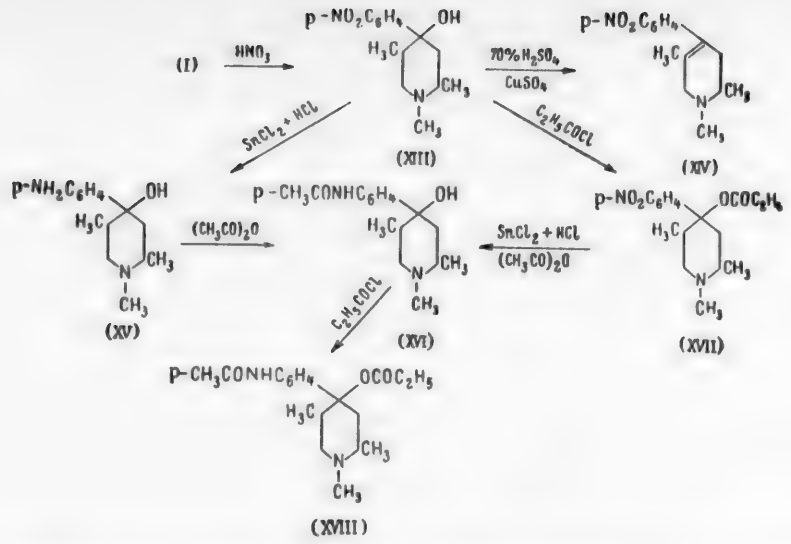
** Transliteration of Russian, commonly known in USA as pontocain hydrochloride or tetracaine hydrochloride – Publisher's note.

Compound	Activity index at concentration		Toxicity LD_{50} (mg/kg)
	0.1%	0.5%	
Dikain 	683	—	10
(II)	1300	—	24.5
 (XII)	1300	—	31
 (IV)	—	952	—

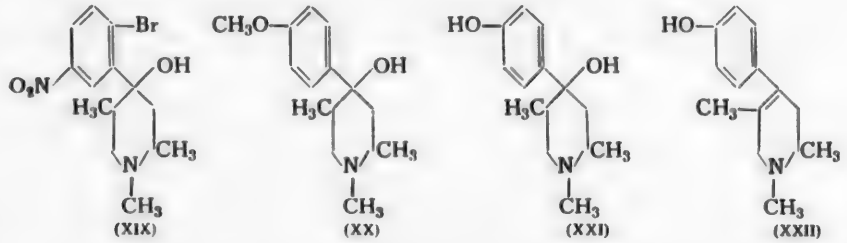
Earlier we had prepared a number of 1,2,5-trimethyl-4-phenyl-4-piperidols [3], containing different substituents in the phenyl radical. The physiological activity of the esters of these substituted 4-phenyl-4-piperidols is frequently quite different from the activity of the analogous esters of 1,2,5-trimethyl-4-phenyl-4-piperidol itself. For example, the propionate of 1,2,5-trimethyl-4-(2'-methoxy-5'-bromophenyl)-4-piperidol, being an analog of promedol, is devoid of analgesic properties, but does show local anesthetic action. In this study we made an attempt to introduce the nitro and amino groups into the aromatic nucleus of 1,2,5-trimethyl-4-phenyl-4-piperidol.

By directly treating the γ-isomer (I) at 50-60° with nitrating mixture we obtained 1,2,5-trimethyl-4-p-nitrophenyl-4-piperidol (XIII) in 40% yield and with m. p. 146-149°, which does not change when heated with 10% alcoholic potassium hydroxide solution. Piperidol (XIII) dehydrates when treated with 70% sulfuric acid in the presence of copper sulfate with the apparent formation of 1,2,5-trimethyl-4-p-nitrophenyl-1,2,3,6-tetrahydropyridine (XIV). Later the nitro group in piperidol (XIII) was reduced using stannous chloride, and here 1,2,5-trimethyl-4-p-aminophenyl-4-piperidol (XV) was obtained in 83% yield. An attempt to replace the amino group in piperidol (XV) by hydroxyl proved unsuccessful. Decomposition of the diazo compound, obtained by treating piperidol (XV) in acid solution with sodium nitrite, proceeds with the copious evolution of nitrogen and is accompanied by tar formation. Similar tar formation is observed when the diazo compound, obtained from piperidol (XV), is coupled with β-naphthol. The bright red solution that is obtained here rapidly darkens, and the desired azo compound cannot be isolated (see diagram on following page).

The reaction of acetic anhydride with 1,2,5-trimethyl-4-p-aminophenyl-4-piperidol (XV) yields 1,2,5-trimethyl-4-p-acetamidophenyl-4-piperidol (XVI), which was also obtained by a different route. Reaction of 1,2,5-trimethyl-4-p-nitrophenyl-4-piperidol (XIII) with propionyl chloride in benzene gave the propionic ester (XVII) of this piperidol. Reduction of the nitro group in the last compound with stannous chloride and concentrated hydrochloric acid in alcohol solution is accompanied by simultaneous saponification of the ester grouping. The resulting piperidol (XV) was not isolated in this case, but instead was immediately treated with acetic anhydride, and this gave the above described 1,2,5-trimethyl-4-p-acetamidophenyl-4-piperidol (XVI). Esterification of piperidol (XVI) with propionyl chloride in benzene gave the propionic ester (XVIII) of 1,2,5-trimethyl-4-p-acetamidophenyl-4-piperidol. In contrast to promedol, propionic ester (XVII), containing a nitro group in the phenyl radical, as well as propionate (XVIII), containing an acetamido group in the phenyl radical, do not show analgesic activity.



The direct nitration of 1,2,5-trimethyl-4-phenyl-4-piperidyl propionate (promedol) is accompanied by strong tarring of the substance. Reaction of p-bromonitrobenzene with butyllithium, and this with 1,2,5-trimethyl-4-piperidone, gave 1,2,5-trimethyl-4-(2'-bromo-5'-nitrophenyl)-4-piperidol (XIX) in very low yield (about 1%). We also attempted to prepare 1,2,5-trimethyl-4-p-hydroxyphenyl-4-piperdol (XXI) by heating 1,2,5-trimethyl-4-p-methoxyphenyl-4-piperidol (XX) with concentrated hydrobromic acid. However, this reaction is accompanied by dehydration, and instead of piperidol (XXI), we isolated 1,2,5-trimethyl-4-p-hydroxyphenyl-1,2,3,6-tetrahydropyridine (XXII).



The complete results of the pharmacological testing of the obtained compounds will be published in a separate communication.

EXPERIMENTAL

For the esterifications we used γ-isomer of 1,2,5-trimethyl-4-phenyl-4-piperidol (m. p. 107-108°), described in previous communications [1,4].

1,2,5-Trimethyl-4-phenyl-4-piperidyl p-methoxyphenoxyacetate (II). A mixture of 7.9 g of (I), 10 ml of dry benzene and 14 g of freshly distilled p-methoxyphenoxyacetyl chloride (b. p. 136-138° at 8 mm) was heated for 4 hrs on the water bath. The obtained crystalline precipitate was filtered the next day and repeatedly washed with benzene. After drying we obtained 10.7 g of the hydrochloride of ester (II), which after two recrystallizations from acetone melted at 189-190°.

Found %: N 3.44, 3.61. $C_{23}H_{30}O_4NCl$. Calculated %: N 3.50.

1,2,5-Trimethyl-4-phenyl-4-piperidyl p-ethoxyphenoxyacetate (III). For reaction we took 6 g of (I), 7 ml of dry benzene and 12 g of freshly distilled p-ethoxyphenoxyacetyl chloride (b. p. 148-149° at 9 mm). The reaction was run in the same manner as above. After two recrystallizations from acetone we obtained 3.4 g of the hydrochloride of ester (III) with m. p. 195-196°.

Found %: N 3.33, 3.41. $C_{24}H_{32}O_4NCl$. Calculated %: N 3.22.

1,2,5-Trimethyl-4-phenyl-4-piperidyl α-phenoxypropionate (IV). To a solution of 3 g of (I) in 5 ml of benzene with cooling and stirring was gradually added 6 g of freshly distilled α-phenoxypropionyl chloride (b. p. 124° at 3 mm). The mixture was heated for 10 hrs on the water bath. The benzene was vacuum-distilled from the extremely dark reaction mixture. The residue was dissolved in water and treated with saturated soda solution. The organic bases that separated here were extracted with ether, dried over sodium sulfate, and fractionally distilled in vacuo. We obtained two fractions: 1st fraction, b. p. 113-120° at 2.5 mm, 0.4 g; 2nd fraction, 160-182° at 2.5 mm, 2.1 g. Dry hydrogen chloride was passed into an ether solution of the 2nd fraction. The resulting precipitate of ester (IV) hydrochloride was dissolved in acetone and again precipitated with ether. An attempt to recrystallize ester (IV) hydrochloride from various solvents proved unsuccessful. The substance represents colorless crystals, melting at 90° with effervescence.

Found %: N 3.80, 3.82. $C_{23}H_{30}O_3NCl$. Calculated %: N 3.47.

1,2,5-Trimethyl-4-phenyl-4-piperidyl α-phenoxyisobutyrate (V). This ester could not be obtained by the direct esterification of piperidol (I) with α-phenoxyisobutyric chloride, using the technique of the preceding experiments. The esterification hardly goes under mild conditions, while long heating at elevated temperature (111-120°) causes pronounced tarring of the reaction mass. A similar situation was also observed by us earlier when we attempted to esterify piperidol (I) with acids having a branched carbon chain. Thus, for example, we were unable to obtain the trimethylacetic and isobutyric esters by this technique. Esterification is also difficult in the case of reacting piperidol (I) with isovaleryl chloride. The isobutyric and isovaleric esters were obtained [1] through the lithium alcoholate of piperidol (I). This method was also used to obtain the ester described below (V).

The lithium alcoholate of 1,2,5-trimethyl-4-phenyl-4-piperidol was prepared from 1 g of lithium, 15.3 g of bromobenzene and 8.5 g of 1,2.5-trimethyl-4-piperidone in 200 ml of absolute ether. Then to the reaction mass with vigorous stirring was added 24 g of α-phenoxyisobutyryl chloride (b. p. 101° at 8 mm). The mixture was heated at ether boil for 4 hrs and then 50 ml of water was added, the ether layer separated, and the lower water layer treated with soda. The organic bases that separated here were extracted with ether, dried, and vacuum-distilled. The following fractions were obtained: 1st fraction, b. p. 143-175° at 2.5 mm, 8 g; 2nd fraction, 175-186° at 2.5 mm, 29 g. From 0.7 g of the 2nd fraction we obtained 0.8 g of the picrate of ester (V) with m. p. 190-191° (from alcohol).

Found %: N 9.27, 9.51. $C_{30}H_{34}O_{10}N_4$. Calculated %: N 9.18.

The passage of hydrogen chloride into an ether solution of the 2nd fraction gave the hydrochloride as a viscous precipitate, which could not be made to crystallize.

1,2,5-Trimethyl-4-phenyl-4-piperidyl α-p-chlorophenoxyisobutyrate (VI). A mixture of 8 g of (I), 8 ml of dry benzene and 17.5 g of α-p-chlorophenoxyisobutyryl chloride (b. p. 130-131° at 10 mm) was heated for 4 hrs on the water bath. The benzene was vacuum-distilled from the dark reaction mass, and the residue was treated with soda to give the free organic bases. Vacuum-distillation of the bases gave a fraction with b. p. 190-230° at 2 mm (2.7 g), from which the picrate of ester (VI) with m. p. 150-152° (from alcohol) was isolated.

Found %: N 9.38, 9.15. $C_{30}H_{33}O_{10}N_4Cl$. Calculated %: N 8.68.

The hydrochloride of this ester was obtained as a noncrystallizing oil.

1,2,5-Trimethyl-4-phenyl-4-piperidol p-nitrophenoxyacetate (VII). A mixture of 10 g of (I), 15 ml of dry benzene, 0.1 g of magnesium and 21.1 g of p-nitrophenoxyacetyl chloride (m. p. 84-87.5°) was heated for 8 hrs at 70-80°. The next day the obtained precipitate was filtered and washed with acetone. We obtained 3.8 g of the hydrochloride of ester (VII), which after two recrystallizations from acetone melted at 186-188°.

Found %: N 6.07, 6.28; C 60.36, 60.79; H 5.81, 5.91. $C_{22}H_{27}O_5N_2Cl$. Calculated %: N 6.44; C 60.75; H 5.98.

1,2,5-Trimethyl-4-phenyl-4-piperidyl p-aminophenoxyacetate (VIII). A solution of 12 g of stannous chloride in 15 ml of alcohol and 15 ml of concentrated hydrochloric acid was gradually added to a solution of 3 g of of ester (VII) hydrochloride in 50 ml of anhydrous ethanol at 50°. The mixture was heated on the water bath at 80° for 5 hrs. The alcohol was distilled under slight vacuum, and the residue was dissolved in water and treated with soda. The obtained oily layer of organic bases was extracted with ether, the ether solution dried, and then dry hydrogen chloride was passed into it. The obtained precipitate was recrystallized from acetone to give 0.4 g of ester (VIII) dihydrochloride with m. p. 155-156°.

Found %: N 6.60, 6.32. $C_{22}H_{30}O_3N_2Cl_2$. Calculated %: N 6.35.

1,2,5-Trimethyl-4-phenyl-4-piperidyl diphenylacetate (IX). A mixture of 3 g of (I), 5 ml of benzene and 14 g of diphenylacetyl chloride (b. p. 115-118° at 2.5 mm) was heated for 5 hrs at 70-80°. The product was diluted with absolute ether, the separated oil repeatedly washed with ether, and then dissolved in water. The aqueous solution was washed with ether, treated with dilute ammonia solution, the organic bases extracted with ether, the ether solution dried, and then treated with dry hydrogen chloride. The obtained crystals were recrystallized from acetone to give 2 g of ester (IX) hydrochloride with m. p. 194-195°.

Found %: N 2.99, 3.18. $C_{28}H_{32}O_2NCl$. Calculated %: N 3.11.

1,2,5-Trimethyl-4-phenyl-4-piperidyl phenylpropiolate (X). For reaction we took 3 g of (I), 4 ml of benzene and 4 g of phenylpropioloyl chloride (b. p. 111-113° at 15 mm). Much evolution of heat was observed during the addition of the chloride. The reaction mass was cooled in ice water, the voluminous crystalline precipitate filtered, washed on the filter with benzene, and recrystallized from acetone. We obtained 2.3 g of ester (X) hydrochloride with m. p. 169-170°.

Found %: N 3.41, 3.41. $C_{23}H_{26}O_2NCl$. Calculated %: N 3.65.

1,2,5-Trimethyl-4-phenyl-4-piperidyl pyromucate (XI). A mixture of 5 g of (I), 7.5 ml of benzene and 7.5 g of pyromucyl (2-furoyl) chloride (b. p. 72-73° at 18 mm) was heated at 70-80° for 3 hrs. After recrystallization from acetone, the obtained precipitate (4.2 g) of ester (XI) hydrochloride melted at 206-207°.

Found %: N 3.87, 4.20. $C_{19}H_{24}O_3NCl$. Calculated %: N 4.00.

The mother liquor from the above precipitate (4.2 g) was treated in conventional manner to give 3.4 g of the free ester (XI) with m. p. 92-94° (from benzine*).

Found %: N 4.59, 4.63. $C_{19}H_{23}O_3N$. Calculated %: N 4.47.

1,2,5-Trimethyl-4-phenyl-4-piperidyl β-phenylmercaptopropionate (XII). a) β-Phenylmercaptopropionyl chloride. To 20 g of thiophenol was added two drops of a saturated alcoholic solution of sodium ethylate, and then 16 g of acrylonitrile was gradually added with cooling. The mixture was heated for 8 hrs at 50° and for 2 hrs in a boiling water bath. Distillation gave 27 g of β-phenylmercaptopropionitrile with b. p. 111-112° at 3 mm, which was heated for 4 hrs on the water bath (80-90°) with 35 g of concentrated hydrochloric acid under vigorous stirring. The mixture after cooling was treated with 50 ml of water, and the obtained precipitate was extracted with ether. We obtained 30 g of β-phenylmercaptopropionic acid with m. p. 58-59° (from water), which was treated with 50 ml of thionyl chloride, and after conventional treatment we obtained 27.5 g of β-phenylmercaptopropionyl chloride with b. p. 139° at 4 mm.

b) 1,2,5-Trimethyl-4-phenyl-4-piperidyl β-phenylmercaptopropionate (XII). A mixture of 7 g of (I), 10 ml of dry benzene and 17 g of β-phenylmercaptopropionyl chloride was heated for 10 hrs at vigorous benzene reflux. The benzene was vacuum-distilled, and the residue was treated with 30 ml of water and 30 ml of ether. A dark viscous oil, insoluble in both water and ether, settled on the bottom of the flask, which was separated and treated with dilute ammonia solution in the presence of ether. The ether extract of the bases was dried over sodium sulfate and then treated with hydrogen chloride to give an oil, readily soluble in acetone and benzene. Recrystallization from benzene gave 0.5 g of ester (XII) hydrochloride with m. p. 158-161°.

Found %: N 3.55, 3.53. $C_{23}H_{30}O_2NSCl$. Calculated %: N 3.33.

1,2,5-Trimethyl-4-p-nitrophenyl-4-piperidol (XIII). 3 g of (I) was added in small portions to a mixture of 1.6 ml of nitric acid (d 1.36) and 2 ml of sulfuric acid (d 1.84). After heating on the water bath for 45 min at

* As in original – Publisher's note.

60° the reaction mass was poured into 50 ml of cold water. The aqueous solution was treated with soda, and the organic bases were extracted with ether and dried over sodium sulfate. Removal of the ether by distillation gave 3.2 g of residue, which recrystallized from benzine* gave 1 g of (XIII) with m. p. 146-149°.

Found %: N 10.65, 10.66. $C_{14}H_{20}O_3N_2$. Calculated %: N 10.60.

1,2,5-Trimethyl-4-p-nitrophenyl-1,2,3,6-tetrahydropyridine (XIV). A mixture of 2 g of (XIII), 3.5 g of 70% sulfuric acid and 0.5 g of fused copper sulfate was heated for 4 hrs in a boiling water bath. Treatment with water and extraction with ether gave 1.5 g of (XIV) as a mobile liquid, from which the picrate with m. p. 155-157° (from alcohol) was obtained.

Found %: N 14.92, 14.84. $C_{20}H_{21}O_9N_5$. Calculated %: N 14.72.

1,2,5-Trimethyl-4-p-aminophenyl-4-piperidol (XV). A solution of 10 g of stannous chloride in 15 ml of alcohol and 15 ml of concentrated hydrochloric acid was gradually added to a solution of 2.8 g of (XIII) in 50 ml of anhydrous alcohol heated to 50°. After heating for 6 hrs on the water bath the solvent was distilled off, and the residue was dissolved in water and treated with potassium hydroxide. The free base that separated here was extracted with ether, dried over sodium sulfate, and then fractionally distilled to give 2 g of (XV) with m. p. 139-140° (from benzine).

Found %: N 11.72, 11.80. $C_{14}H_{22}ON_2$. Calculated %: N 11.53.

1,2,5-Trimethyl-4-p-acetamidophenyl-4-piperidol (XVI). a) A solution of 0.2 g of (XV) in 20 ml of 5% hydrochloric acid was treated at 50° with 1 ml of acetic anhydride. The product was treated with saturated soda solution, extracted with ether, and the ether partially evaporated to give 0.15 ml of (XVI) as crystals with m. p. 231-233°.

Found %: N 10.18, 10.03. $C_{16}H_{24}O_2N_2$. Calculated %: N 10.01.

b) 3 g of the propionate (XVII) hydrochloride was reduced with stannous chloride (12 g) in an alcoholic solution of concentrated hydrochloric acid (alcohol 65 ml, acid 15 ml) at the boil for 5 hrs. We obtained 2.7 g of reduction product, which without purification was acetylated with acetic anhydride (1.6 g) by the above-described procedure. We obtained 1.5 g of (XVI) with m. p. 231-233°, failing to depress the melting point when mixed with the above-obtained specimen.

1,2,5-Trimethyl-4- p-nitrophenyl-4-piperidyl propionate (XVII). A mixture of 3 g of (XIII), 5 ml of dry benzene and 3 ml of propionyl chloride was heated at benzene boil for 3 hrs. The flask contents crystallized on cooling. The crystals were separated, washed with benzene, and recrystallized twice from acetone. We obtained 1.8 g of propionate (XVII) hydrochloride with m. p. 244-245.5°.

Found %: N 7.90, 7.63. $C_{17}H_{25}O_4N_2Cl$. Calculated %: N 7.85.

1,2,5-Trimethyl-4-p-acetamidophenyl-4-piperidyl propionate (XVIII). A mixture of 1.5 g of (XVI), 6 ml of dry benzene and 2 ml of propionyl chloride was heated for 4 hrs at benzene reflux. The benzene together with excess propionyl chloride was decanted, while the residual oil was dried in a vacuum-desiccator and then dissolved in acetone. Treatment of the acetone solution with absolute ether gave colorless crystals (0.9 g) of propionate (XVIII) hydrochloride, melting at 70° (with decomp.).

Found %: N 7.72, 7.46. $C_{19}H_{29}O_3N_2Cl$. Calculated %: N 7.59.

1,2,5-Trimethyl-4-(2'-bromo-5'-nitrophenyl)-4-piperidol (XIX). To the butyllithium, obtained from 7.2 g of lithium and 50 g of butyl bromide in 300 ml of absolute ether, was added with cooling in ice water a solution of 52.5 g of p-bromonitrobenzene (m. p. 125-126°) in 200 ml of ether. After vigorous stirring for 1 hr, 36 g of 1,2,5-trimethyl-4-piperidone was added in drops. The product was treated with water (50 ml) and 18% hydrochloric acid (170 ml). The water layer was treated with potassium hydroxide, and the bases that separated here were extracted with ether, dried, and vacuum-distilled. We obtained 25.6 g of 1,2,5-trimethyl-4-piperidone and 1 g of a fraction with b. p. 160° at 3 mm, which crystallized in the receiver. Recrystallization from bezine gave 0.3 g of (XIX) as orange crystals with m. p. 192-195°.

Found %: N 8.24, 8.41. $C_{14}H_{19}O_3N_2Br$. Calculated %: N 8.17.

* As in original – Publisher's note.

1,2,5-Trimethyl-4-p-hydroxyphenyl-1,2,3,6-tetrahydropyridine (XXII). A mixture of 2 g of (XX) (m. p. 99-100°) [3], 15 ml of concentrated hydrobromic acid and 20 ml of glacial acetic acid was heated in a boiling water bath for 5 hrs. The acids were vacuum-distilled, while the residue was dissolved in water and treated with sodium hydroxide. The ether extract of organic bases was dried over fused sodium sulfate. Removal of the ether by distillation left 0.5 g of mobile liquid, from which the picrate of (XXII) with m. p. 134-136° (from alcohol) was obtained.

Found %: N 12.70, 12.46. $C_{20}H_{22}O_8N_4$. Calculated %: N 12.56.

SUMMARY

For the purpose of pharmacological testing and to study the relationship between the structure and physiological action of esters of 4-aryl-4-piperidols we synthesized a new series of compounds of this type. Two of the synthesized esters, namely the β-phenylmercaptopropionic and p-methoxyphenoxyacetic esters of 1,2,5-trimethyl-4-phenyl-4-piperidol, show a high anesthetic activity and a comparatively low toxicity.

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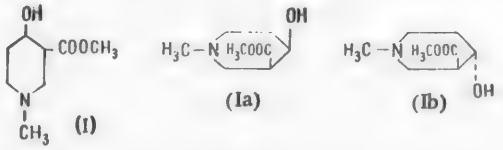
SYNTHESIS OF N-METHYL-3-CARBOMETHOXY-4-HYDROXYPIPERIDINES AND A STUDY OF THEIR STERIC STRUCTURES

M. E. Maurit and N. A. Preobrazhenskii

In our paper on the synthesis of arecoline and its homologs [1] we described the preparation of this alkaloid from methyl acrylate and from acrylonitrile. The intermediate in this synthesis is N-methyl-3-carbomethoxy-4-hydroxypiperidine (I). As can be seen from the given formula, piperidol (I) has two asymmetric carbon atoms, and according to theory it is possible for two racemic stereoisomers (Ia) (cis-3:4) and (Ib) (trans-3:4) to exist.



In this paper we investigated various methods for the reduction of N-methyl-3-carbomethoxy-4-piperidone (II) to the corresponding piperidol (Ia, Ib), the separation of the isomeric piperidols, and the conditions of their dehydration.

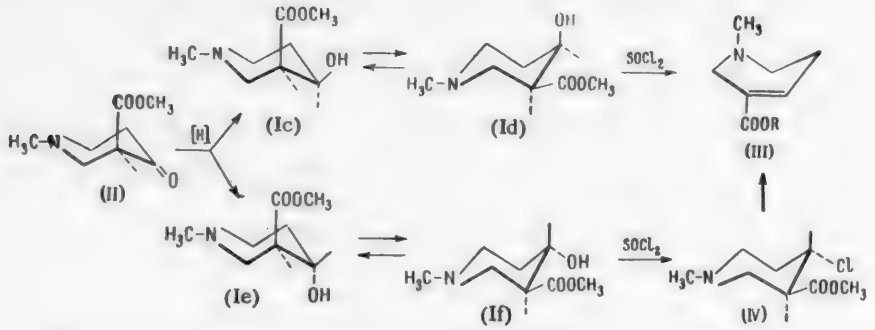
The catalytic reduction of ketone (II) using skeletal nickel catalyst gave chiefly one isomer with m. p. 86-87°, the hydrobromide of which had m. p. 144.5-145.5°. Reduction using sodium amalgam gave a mixture of piperidols with m. p. 65-68°, which was separated by recrystallizing their hydrobromides from either anhydrous ethyl or isopropyl alcohol. Here we isolated a piperidol hydrobromide with m. p. 181-182° (30%), from which a base with m. p. 96-97° was obtained, and a second hydrobromide with m. p. 142-143° (19%), corresponding to the base with m. p. 86-87°.

Electrochemical reduction at a lead cathode in alkaline medium gave a mixture of hydrochlorides of the isomeric N-methyl-4-hydroxyhexahydronicotinic acids, which by conventional esterification was converted into the methyl esters of the corresponding bases. From this mixture of piperidols, having m. p. 72-77°, we also obtained two hydrobromides, one with m. p. 182-182.5° (12%) and the other with m. p. 143-144° (18.8%). The mixed melting point of the piperidol hydrobromides with m. p. 144.5-145.5° and 182-182.5° is 130-152°, and that of the free bases with m. p. 86-87° and 96-97° is 67-70°.

When the reaction of the isomeric N-methyl-3-carbomethoxy-4-hydroxypiperidines with thionyl chloride was investigated, we found that the piperidol with m. p. 86-87° is easily dehydrated to yield arecoline (III, R = = CH_3), whereas the piperidol with m. p. 96-97° is converted to N-methyl-3-carbomethoxy-4-chloropiperidine (IV). Chloro derivative (IV), having the same configuration as the starting hydroxy compound (Ib), apparently suffers Walden inversion when treated with alkali and cleaves a molecule of hydrogen chloride, in which connection the ester group is saponified at the same time to yield arecaidine (III, R = H), which we isolated and identified as the hydrochloride.

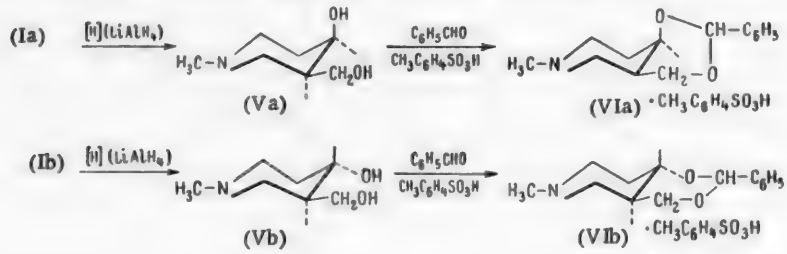
Consequently, based on the differences between the piperidol with m. p. 86-87° and the piperidol with m. p. 96-97, the N-methyl-3-carbomethoxy-4-hydroxypiperidines show cis (Ia)-trans (Ib) isomerism. However, the answer to the question as to which configuration corresponds to the hydroxy derivative with m. p. 86-87° or with m. p. 96-97° presents greater difficulties. Since water is usually cleaved more easily from a cis-isomer than

from the trans-isomer, and since compounds of the cis-series have lower melting and boiling points than do trans-compounds, then the piperidol with m. p. 86-87° must be the cis-isomer (Ia), and the piperidol with m. p. 96-97° the trans-isomer (Ib).



To support this position we adopted the method used by G. Fodor to establish spatial configuration in the series of tropane alkaloids [2]. Both piperidol isomers were reduced with aluminum lithium hydride to the corresponding diols (Va and Vb), which when reacted with benzaldehyde in the presence of toluenesulfonic acid both gave O,O'-benzylidene-N-methylpiperidine-3-hydroxymethyl-4-ol toluenesulfonates (VIa and VIb) with m. p. 173-174° and 200-202°, respectively. The mixed melting point of these salts was 168-170°.

As a result, it proved that both of the piperidol stereoisomers can give benzylidene derivatives, in contrast to the cis- and trans- derivatives described by G. Fodor in the tropane series. This tendency to form cyclic acetals can be explained on the basis of the conformation of both the cis-3:4 (Ic, Id) and trans-3:4 (Ie, If) N-methyl-3-carbomethoxy-4-hydroxypiperidols. From the presented formulas it can be seen that for both the cis- and trans-isomers it is possible to have such structure conformations as to put the hydroxyl groups sufficiently close to each other to permit forming the six-membered ring of the benzylidene derivative.



EXPERIMENTAL

1. Methyl esters of isomeric N-methyl-4-hydroxypiperidine-3-carboxylic acids. a) Catalytic reduction. The reduction of N-methyl-3-carbomethoxy-4-piperidone (II) in the presence of skeletal nickel catalyst was run in the same manner as described in the previous paper [1]. We obtained 34.8 g of piperidol (Ia) from 51.3 g of technical ketone (II) (67% yield, based on ketone). B. p. 114-118° at 8 mm. The free piperidol base (Ia) was recrystallized from anhydrous ethyl alcohol. M. p. 86-87°.

Hydrobromide of piperidol (Ia). A solution of 8.66 g of the free piperidol base (Ia) in 20 ml of anhydrous alcohol was treated at 0° with an alcoholic solution of hydrogen bromide (until acid to Congo). The mixture was cooled to −10° and the obtained crystals were filtered. M. p. 142-144°. Yield 11.7 g (92.1%); after recrystallization from anhydrous ethyl alcohol (1 : 3) the compound melted at 144.5-145.5°.

Found %: C 37.92, 37.97; H 6.15, 6.20; N 5.37, 5.31; Br 31.60. $C_8H_{15}O_3N \cdot HBr$. Calculated %: C 37.83; H 6.35; N 5.51; Br 31.45.

Free base N-methyl-3-carbomethoxy-4-hydroxypiperidine (Ia) from the hydrobromide with m. p. 144.5-145.5°. A solution of 9 g of piperidol (Ia) hydrobromide with m. p. 144.5-145.5° in 6 ml of water was made alkaline with ammonia solution. The free base was extracted with chloroform. Yield 6 g (97.8%). M. p. 86-87°.

Found %: C 55.42; H 8.45; N 7.92, 8.01. $C_8H_{15}O_3N$. Calculated %: C 55.49; H 8.73; N 8.09.

b) Electrochemical reduction at lead cathode in alkaline medium. A water solution of the sodio derivative of N-methyl-3-carbomethoxy-4-piperidone (II), obtained from the cyclization of 46.5 g of β,β'-dicarbomethoxydiethylmethylamine, was placed in a porous beaker and subjected to reduction at a lead cathode with a current strength of 7-8 amp, a potential difference of 5-6 v and a temperature of 18-20° for 10-12 hrs. Both the cyclization and the reduction were run by the method described in the previous paper [1]. The solution obtained after reduction was acidified with hydrochloric acid and then evaporated in vacuo. The hydrochlorides of the N-methyl-4-hydroxyhexahydronicotinic acids were extracted from the dry residue with hot methyl alcohol (3 times with 70 ml portions). Then the extract was treated with 10 ml of concentrated sulfuric acid and the whole heated at the boil for 5 hrs, after which the excess alcohol was distilled off, the residue neutralized with saturated potash solution (to phenolphthalein) with efficient cooling, and the piperidols (Ia and Ib) extracted with chloroform (3 times with 30 ml portions). The solvent was distilled off, and the residue was vacuum-distilled. Yield of N-methyl-3-carbomethoxy-4-hydroxypiperidines (Ia and Ib) 21.5 g (54.2%), based on β,β'-dicarbomethoxydiethylmethylamine. B. p. 110-122° at 8 mm. The piperidols were recrystallized from anhydrous ethyl alcohol. M. p. 72-77°.

Found %: C 55.27; H 8.50; N 7.97. $C_8H_{15}O_3N$. Calculated %: C 55.49; H 8.73; N 8.09.

The mixed melting point of piperidol (Ia) with m. p. 86-87° (from catalytic reduction) and mixture (Ia and Ib) of piperidols with m. p. 72-77° (from electrochemical reduction) was 72-80°.

Hydrobromides of piperidols (Ib and Ia). The mixed piperidols (21.5 g) with m. p. 72-77°, obtained from electrochemical reduction, were converted to the hydrobromides in the same manner as described above for the free piperidol base (I) obtained after catalytic reduction. The yield of mixed N-methyl-3-carbomethoxy-4-hydroxypiperidine hydrobromides was 30.8 g (97.6%). M. p. 128-135°.

After 1 recrystallization from 15 volumes of anhydrous alcohol and 2 recrystallizations from 20 volumes we obtained 3.7 g of piperidol (Ib) hydrobromide (12% of the total amount of hydrobromides). M. p. 182-182.5°.

Found %: C 37.64; H 6.45; N 5.32, 5.48; Br 31.36. $C_8H_{15}O_3N \cdot HBr$. Calculated %: C 37.83; H 6.35; N 5.51; Br 31.45.

The mother liquors from the recrystallizations were distilled to remove solvent and the residual hydrobromide was recrystallized from anhydrous isopropyl alcohol (1:1). The yield of piperidol (Ia) hydrobromide with m. p. 143-144.5° was 8 g (18.8% of the total amount of hydrobromides). The mixed melting point of the piperidol hydrobromides with m. p. 144.5-145.5° (from catalytic reduction) and with m. p. 182-182.5° (from electrochemical reduction) was 130-152°.

Free base N-methyl-3-carbomethoxy-4-hydroxypiperidine (Ib) from piperidol (Ib) hydrobromide with m. p. 182-182.5°. From 7.6 g of piperidol (Ib) hydrobromide with m. p. 182-182.5° we isolated 4.94 g (95.4%) of free piperidol base (Ib), which was recrystallized from anhydrous alcohol. M. p. 96.5-97.5°.

Found %: C 55.65, 55.37; H 8.57, 8.57; N 8.32, 8.02. $C_8H_{15}O_3N$. Calculated %: C 55.49; H 8.73; N 8.09.

The mixed melting point of the piperidols with m. p. 86-87° and with m. p. 96.5-97.5° was 67-70°.

Reduction with sodium amalgam. To a solution of 17 g of N-methyl-3-carbomethoxy-4-piperidone hydrochloride (II · HCl) in 170 ml of water and 10 ml of concentrated hydrochloric acid was gradually added with vigorous stirring, at −2 to 0°, 930 g of 5% sodium amalgam (in portions of 19 g every 5-10 min). The reaction solution was maintained constantly acid by the addition of 200 ml of concentrated hydrochloric acid. When reduction was complete, which was established by testing with ferric chloride, the settled solution was decanted from the mercury, made alkaline with saturated potash solution (to phenolphthalein), and the free piperidols (Ia and Ib) extracted with chloroform (4 times with 40 ml portions). The solvent was distilled off, and the residue was vacuum-distilled. The yield of N-methyl-3-carbomethoxy-4-hydroxypiperidines (Ia and Ib) was 8.8 g (62.1%, based on ketone hydrochloride). B. p. 110-117° at 7 mm. The mixed piperidols were recrystallized from alcohol. M. p. 65-68°.

Hydrobromides of piperidols (Ia and Ib). From 7.5 g of mixed piperidols with m. p. 65-68°, obtained from reduction with sodium amalgam, we isolated 3.3 g of piperidol (Ib) hydrobromide with m. p. 181-182° (30%, based on the free base) and 2.1 g of piperidol (Ia) hydrobromide with m. p. 142-143° (19%). From the first hydrobromide we obtained the free piperidol (Ib) with m. p. 96-97°, and from the second – the free base (Ia) with m. p. 86-87°.

2. Reaction of thionyl chloride with isomeric piperidols (Ia and Ib). a) Free arecoline (III, R = CH_3). A solution of 3 g of free piperidol (Ia) with m. p. 86-87° in 15 ml of dry benzene was treated with 6 ml of thionyl chloride under cooling. After standing for 1 hr at room temperature the reaction mass was heated at reflux for 3 hrs, then the excess thionyl chloride and solvent were removed in vacuo, the residue dissolved in 5 ml of water, the solution made alkaline with aqueous ammonia, and the free arecoline extracted with ether (4 times with 5 ml portions). The extract was dried over sodium sulfate, the solvent distilled off, and the residue vacuum-distilled. The yield of arecoline as the free base was 1.7 g (63.2%, based on piperidol Ia).

B. p. 92-93° at 7 mm; $n^{20}D$ 1.4302, d^{20}_4 1.0495, MR_D 42.06. $C_8H_{13}O_2N$. Calculated 42.07.

Arecoline hydrobromide melts at 169-170°. Its mixture with the hydrobromide of the natural alkaloid (m. p. 169-170.5°) fails to show a melting point depression.

b) N-Methyl-3-carbomethoxy-4-chloropiperidine (IV). A solution of 2 g of free piperidol (Ib) with m. p. 96.5-97.5° (isolated from the hydrobromide with m. p. 182-182.5°) in 20 ml of benzene was treated with 4 ml of thionyl chloride. The remainder of the process was run in the same manner as described above for the isomeric piperidol (Ia) with m. p. 86-87°. Removal of the ether by distillation left the technical N-methyl-3-carbomethoxy-4-chloropiperidine (IV). Yield 2.15 g (97.2%, based on free piperidol Ib). M. p. 160-162°.

Chloro derivative (IV) was recrystallized from anhydrous ethyl alcohol (1:3). M. p. 161-162°.

Found %: C 50.32, 49.96; H 7.32, 7.26; N 7.17; Cl 18.41, 18.39. $C_8H_{14}O_2NCl$. Calculated %: C 50.16; H 7.38; N 7.31; Cl 18.50.

c) Arecaidine hydrochloride (III, R = H · HCl). A solution of 0.8 g of N-methyl-3-carbomethoxy-4-chloropiperidine (IV) in 5 ml of water was made alkaline with 30% sodium hydroxide solution. After standing for 3 hrs at room temperature the solution was acidified with hydrochloric acid (to Congo) and then evaporated in vacuo. Arecaidine hydrochloride was extracted from the dry residue with hot methyl alcohol. Removal of the solvent by distillation left 0.7 g of technical arecaidine hydrochloride (94.4%, based on the chloro derivative) with m. p. 245-248°. After recrystallization from a mixture of 10 ml of ethyl alcohol and 10 ml of methyl alcohol the arecaidine hydrochloride melted at 250.5-251°, and based on the physicochemical data, corresponds to the hydrochloride obtained from the natural alkaloid [3].

Found %: C 47.09; H 6.50; N 7.47, 7.61; Cl 20.41. $C_7H_{11}O_2N \cdot HCl$. Calculated %: C 47.34; H 6.81; N 7.88; Cl 19.96.

3. Isomeric N-methyl-3-hydroxymethyl-4-hydroxypiperidines (Va, Vb). a) A solution of 3 g of free base (Ia) with m. p. 86-87° in 100 ml of dry ether was added in 1 hr to an ether solution of aluminum lithium hydride (240 ml of solution containing 0.015 g of aluminum lithium hydride per ml) at −2 to 0°, after which the reaction mass was stirred at room temperature for 4 hrs. Then 7 ml of water was cautiously added with external cooling in ice, the mixture stirred for 1 hr at 18-20°, and the obtained precipitate filtered and washed with anhydrous methyl alcohol (3 times with 10 ml portions). The solvent was removed from the combined extracts by distillation, and the residue was vacuum-distilled. Yield 1.5 g (59.6%, based on free piperidol I); thick viscous oil, readily soluble in water and alcohol, and insoluble in ether, benzene and chloroform. B. p. 154-155° at 7 mm, $n^{20}D$ 1.5058.

Found %: C 58.18, 58.06; H 10.29, 10.55; N 9.32, 9.18. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41; N 9.65.

N-Methyl-3-hydroxymethyl-4-hydroxypiperidine hydrobromide (Va · HBr) was obtained as colorless crystals, readily soluble in water and hot alcohol, more difficultly soluble in cold alcohol, and insoluble in ether. M. p. 136-136.5°.

Found %: C 36.90, 37.24; H 7.14, 7.18; N 6.43, 6.06; Br 35.56, 35.46. $C_7H_{15}O_2N \cdot HBr$. Calculated %: C 37.18; H 7.12; N 6.20; Br 35.34.

b) From 2.4 g of free N-methyl-3-carbomethoxy-4-hydroxypiperidine (Ib) with m. p. 95.5-96.5° we obtained in a similar manner 1.3 g (64.6%) of free N-methyl-3-hydroxymethyl-4-hydroxypiperidine (Vb). Colorless viscous oil, readily soluble in water and alcohol, and insoluble in ether, chloroform and benzene. The compound crystallized on standing. B. p. 156-157° at 7 mm, $n^{20}D$ 1.5026; b. p. 67-68°.

Found %: C 58.09, 57.97; H 10.08, 10.29; N 9.42, 9.50. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41; N 9.65.

N-Methyl-3-hydroxymethyl-4-hydroxypiperidine hydrobromide (Vb · HBr) was obtained as colorless crystals, readily soluble in water and hot alcohol, more difficultly soluble in cold alcohol, and deliquescent in the air. M. p. 138-140° (softens at 75°).

Found %: C 37.47, 37.20; H 6.94, 7.20; N 6.14, 5.91; Br 34.80, 35.22. $C_7H_{15}O_2N \cdot HBr$. Calculated %: C 37.18; H 7.12; N 6.20; Br 35.34.

The mixed melting point of the diol hydrobromides (Va · HBr) with m. p. 136-136.5° and (Vb · HBr) with m. p. 138-140° was 118-120° (softens at 55°).

4. Isomeric O,O'-benzylidene-N-methylpiperidine-3-hydroxymethyl-4-ol toluenesulfonates (VIa and VIb). A mixture of 0.58 g of free N-methyl-3-hydroxymethyl-4-hydroxypiperidine (Va), obtained from the free piperidol (Ia) with m. p. 86-87°, 6 ml of freshly distilled benzaldehyde and 0.83 g of toluenesulfonic acid was heated at 40 mm and a temperature of 85° for 5 hrs, and here some of the benzaldehyde distilled into the sulfuric acid. Since crystallization failed to occur on cooling, the excess benzaldehyde was vacuum-distilled at 10 mm and a bath temperature not exceeding 75°. The residue was treated with 2 ml of anhydrous alcohol and 10 ml of dry ether and the obtained crystals were filtered. The yield of O,O'-benzylidene toluenesulfonate derivative (VIa) was 1.5 g (92.6%). The toluenesulfonate was recrystallized from anhydrous alcohol. M. p. 173-174°.

Found %: C 62.35, 62.11; H 6.69, 6.37; N 3.51, 3.53. $C_{21}H_{27}O_5NS$. Calculated %: C 62.20; H 6.71; N 3.45.

b) A mixture of 0.43 g of free N-methyl-3-hydroxymethyl-4-hydroxypiperidine (Vb), obtained from the free piperidol (Ib) with m. p. 96.5-97.5°, 5 ml of benzaldehyde and 0.62 g of toluenesulfonic acid was heated in vacuo at 85° and 40 mm for 5 hrs. The crystals obtained on cooling were filtered, washed with ether, and recrystallized from anhydrous alcohol. The yield of O,O'-benzylidene toluenesulfonate derivative was 1.1 g (91.6%). M. p. 200-202°.

Found %: C 62.34, 62.14; H 6.89, 6.37; N 3.49, 3.65. $C_{21}H_{27}O_5NS$. Calculated %: C 62.20; H 6.71; N 3.45.

The mixed melting point of the benzylidene toluenesulfonates (VIa) with m. p. 173-174° and (VIb) with m. p. 201-202° was 163-170° (softens at 155°).

SUMMARY

1. Depending on the reducing agent and reduction conditions, it was established that methyl esters of N-methyl-4-hydroxypiperidine-3-carboxylic acid are obtained with a variable relative amount of steric isomers.

2. Two isomers of N-methyl-3-carbomethoxy-4-hydroxypiperidine with m. p. 86-87° and 96.5-97.5° were isolated.

3. In studying the dehydration of the isomeric piperidols with thionyl chloride it was established that the piperidol with m. p. 86-87° gives the base arecoline, while the piperidol with m. p. 96.5-97.5° yields N-methyl-3-carbomethoxy-4-chloropiperidine.

4. The methyl esters of the isomeric N-methyl-3-carboxy-4-piperidols were reduced with aluminum lithium hydride and the obtained isomers of N-methyl-4-hydroxypiperidine were converted to the toluenesulfonates of the isomeric O,O'-benzylidene-N-methylpiperidine-3-hydroxymethyl-4-ols.

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CHEMISTRY OF HETEROCYCLES

XXXII. DI- AND POLYHALO DERIVATIVES OF 9-PHENYLACRIDINE WITH POSITIONS OF HALOGEN IN DIFFERENT BENZENE RINGS

M. E. Konshin and P. A. Petiunin

In previous communications* we described methods for the preparation of mono- and dihalo derivatives of 9-phenylacridine based on 2-aminotriphenylcarbinol and its N-acyl derivatives. Since 9-phenylacridine is a multinuclear heterocycle, then undoubtedly there is interest in utilizing this method to synthesize di- and polyhalo derivatives of 9-phenylacridine with the halogens located in different benzene rings. Another reason for doing this is that compounds of this type are not described in the literature.

The starting di- and polyhalo derivatives of 2-aminotriphenylcarbinol were obtained in satisfactory yields by reacting p-chlorophenylmagnesium bromide with the proper halogenated methyl anthranilate derivatives. The structure and properties of the compounds (I-V) obtained in this manner are given in the table. All of the synthesized compounds are crystalline and show weakly basic properties: they are insoluble in dilute mineral acids and concentrated hydrochloric acid. In addition, compounds (II-V), containing three or more halogen atoms, do not form picrates with picric acid. All of the indicated compounds dissolve in concentrated sulfuric acid with a permanent dark red color. Dilution of such solutions with water results in the separation of the starting halo derivatives of 2-aminotriphenylcarbinol in unchanged form.

It should be mentioned that the basic properties of the halo derivatives of 2-aminotriphenylcarbinol depend to a large extent on the positions of the halogens. The grestest influence is exerted by introducing halogen into the aniline moiety of 2-aminotriphenylcarbinol, and to a lesser degree when halogen is introduced into the other benzene rings.

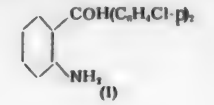
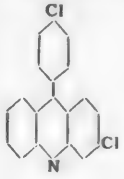
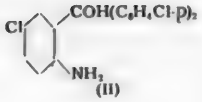
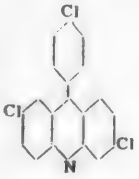
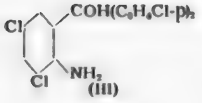
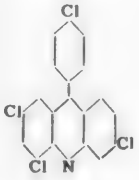
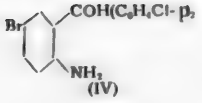
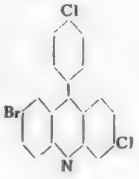
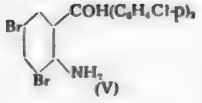
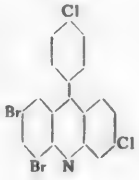
When halo derivatives of 2-aminotriphenylcarbinol (I-V) are heated in nitrobenzene solution they are easily converted into halo derivatives of 9-phenylacridine with the halogens located in different benzene rings (VI-X). The latter are insoluble in dilute mineral acids. They readily dissolve in concentrated sulfuric acid with a yellow-green fluorescence. The basic properties of the acridine bases, the same as in the case of the halo derivatives of 2-aminotriphenylcarbinol, are materially influenced not only by the number of introducted halogen atoms, but also by their location. Thus, for example, compounds containing three halogens atoms in the molecule (VI, VII and IX), in contrast to the 2,4-dihalo derivatives of 9-phenylacridine, form picrates with picric acid. Polyhalo derivatives, containing 4 halogen atoms in the molecule (VIII and IX), do not form picrates. From the data given in the table it can be seen that the melting points of the halo derivatives of 9-phenylacridine increase uniformly with increase in the number of halogen atoms present.

EXPERIMENTAL

4', 4"-Dichloro-2-aminotriphenylcarbinol (I) was obtained by reacting 7.6 g (0.05 mole) of methyl anthranilate with 0.2 g-mole of p-chlorophenylmagnesium bromide. The compound is soluble in alcohol, benzine and acetic acid. It gives a red color with concentrated sulfuric acid. Yield 10.8 g (62.4%). Leaflets (from benzine).

Found %: N 3.84, 4.07; Cl 20.33, 20.52. $C_{19}H_{15}ONCl_2$. Calculated %: N 4.07; Cl 20.62.

* J. Gen. Chem. 27, 475, 1558 (1957).

Halo derivatives of 2-amino-triphenylcarbinol	Melting point	Halo derivatives of 9-phenylacridine		Melting point
 (I)	116—117°		(VI)	177—178°
 (II)	183—185		(VII)	193—194
 (III)	148—149		(VIII)	245—246
 (IV)	193 (decomp.)		(IX)	205—207
 (V)	150—151.5		(X)	254—255

The picrate was obtained as bright yellow leaflets with m. p. 200° (with decomp.).

4',4",5-Trichloro-2-aminotriphenylcarbinol (II) was obtained by reacting 4.6 g (0.025 g-mole) of methyl 5-chloroanthranilate with 0.1 g-mole of p-chlorophenylmagnesium bromide. The compound is readily soluble in alcohol and acetic acid, and insoluble in ether and benzene. Its solutions in concentrated sulfuric acid are colored red. Yield 9 g (95.8%).

Found %: N 3.64, 3.76. $C_{19}H_{14}ONCl_3$. Calculated %: N 3.74.

3,5,4',4"-Tetrachloro-2-aminotriphenylcarbinol (III). For reactions we took 8.5 g of methyl 3,5-dichloroanthranilate, 21.6 g of p-bromobenzene and 2.7 g of magnesium. Yield 7.5 g (47%). The compound is soluble in alcohol, ether, benzine and acetic acid. It gives a red-brown color with concentrated sulfuric acid. Crystals (from alcohol).

Found %: N 3.28, 3.52. $C_{19}H_{13}ONCl_4$. Calculated %: N 3.39.

5-Bromo-4',4"-dichloro-2-aminotriphenylcarbinol (IV). Starting substances: 9 g of methyl 5-bromoanthranilate, 22.9 g of p-bromobenzene and 2.88 g of magnesium. Yield 10.3 (62.6%). Readily soluble in acetic acid, more difficultly soluble in alcohol, and insoluble in ether. It gives a dark red color with concentrated sulfuric acid. Leaflets (from alcohol).

Found %: N 3.08, 3.11. $C_{19}H_{14}ONCl_2Br$. Calculated %: N 3.31.

3,5-Dibromo-4',4"-dichloro-2-aminotriphenylcarbinol (V). For reaction we took 19.1 g (0.1 mole) of p-bromochlorobenzene, 2.4 g (0.1 mole) of magnesium and 10.3 g (0.033 mole) of methyl 3,5-dibromoanthranilate. The compound is soluble in alcohol, ether, benzine and acetic acid. It gives a red-brown color with concentrated sulfuric acid. Yield 10 g (59.6%). Rhombic crystals (from benzine).

Found %: N 2.47, 2.64. $C_{19}H_{13}ONCl_2Br_2$. Calculated %: N 2.79.

3-Chloro-9-p-chlorophenylacridine (VI) was obtained by heating 1 g of (I) in 2 ml of nitrobenzene for 30 min. The precipitate obtained on cooling was filtered and recrystallized from alcohol. Yield 0.3 g (31.85%). The compound is soluble in alcohol and acetic acid, and readily dissolves in concentrated sulfuric acid with a yellow-green fluorescence. Bright yellow leaflets.

Found %: Cl 21.60, 21.63. $C_{19}H_{11}NCl_2$. Calculated %: Cl 21.89.

The picrate was obtained as yellow needles by mixing alcohol solutions of the compound and picric acid. M. p. 231-233°.

2,6-Dichloro-9-p-chlorophenylacridine (VII) was obtained in the same manner as the preceding from 1 g of (II) in 2 ml of nitrobenzene. Yield 0.3 g (31.6%). Soluble in alcohol and acetic acid, difficultly soluble in concentrated hydrochloric acid, and readily soluble in concentrated sulfuric acid. Its solutions in acids show a yellow-green fluorescence. Bright yellow clusters (from alcohol).

Found %: Cl 29.64, 29.70. $C_{19}H_{10}NCl_3$. Calculated %: Cl 29.68.

The picrate was obtained as yellow clusters (from alcohol) with m. p. 261-263°.

2,4,6-Trichloro-9-p-chlorophenylacridine (VIII). For reaction we took 1 g of (III) and 1 ml of nitrobenzene. Yield 0.54 g (56.7%). Soluble in benzene, acetone and chloroform, and insoluble in alcohol, ether, acetone and dilute mineral acids. Its solutions in concentrated sulfuric acid show a yellow-green fluorescence. Yellow crystals (from nitrobenzene).

Found %: N 3.91. $C_{19}H_9NCl_4$. Calculated %: N 3.56.

2-Bromo-6-chloro-9-p-chlorophenylacridine (IX). Reaction was run with 2.5 g of (IV) in 2.5 ml nitrobenzene The compound is soluble in acetic acid and alcohol, and insoluble in benzene, toluene, ether and dilute mineral acids. With concentrated sulfuric acid it forms solutions with a yellow-green fluorescence. Yield 1.5 g (63%). Golden yellow leaflets (from alcohol).

Found %: N 3.66, 3.72. $C_{19}H_{10}NCl_2Br$. Calculated %: N 3.47.

The picrate was obtained as orange crystals (from alcohol) with m. p. 268° (with decomp.).

2,4-Dibromo-6-chloro-9-p-chlorophenylacridine (X) was obtained from 2 g of (V) in 2 ml of nitrobenzene. Yield 1.2 g (62.5%). Soluble in toluene, chloroform and dioxane, and insoluble in alcohol, acetic acid and dilute mineral acids; it dissolves in concentrated sulfuric acid with a yellow-green fluorescence. Golden yellow leaflets (from toluene).

Found %: N 3.31, 3.19. $C_{19}H_9NCl_2Br_2$. Calculated %: N 2.91.

SUMMARY

1. A number of new polyhalo derivatives of 2-aminotriphenylcarbinol were synthesized by reacting mono- and dihalo derivatives of methyl anthranilate with p-chlorophenylmagnesium bromide, and their properties were studied.

2. Based on halo derivatives of 2-aminotriphenylcarbinol, a method was developed for preparing di- and polyhalo derivatives of 9-phenylacridine with the halogens located in different benzene rings; here we obtained a number of previously unknown compounds and studied their properties.

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STUDY OF THE STEPHEN REACTION*

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In 1925 Stephen described [2] a method of obtaining aldehydes by the reduction of nitriles with stannous chloride in anhydrous ether, saturated with hydrogen chloride, followed by hydrolysis of the intermediate aldimine salt.**

$$RCN \xrightarrow{SnCl_2;\ HCl} [RCH{=}NH]_2 \cdot H_2SnCl_6 \xrightarrow{+H_2O} RCHO$$

This method usually gives good results when preparing aldehydes of the aromatic series, but the yields of aliphatic aldehydes fluctuate greatly and for the most part are quite low [7, 10, 12-16] (the data of Stephen on nearly quantitative yields of such aldehydes as phenylacetaldehyde and cinnamaldehyde could not be duplicated [14, 17]). When other investigators attempted to adapt the Stephen method it was found that the time, indicated by Stephen himself, is slightly too short to achieve complete reaction (see, for example, [14]), and that the procedure originally recommended by him to purify anhydrous stannous chloride cannot be duplicated [18]. The vagueness of Stephen's statements led to the situation that the conditions, chosen by later investigators, were often fortuitous to variable degree; thus, in not a single case was the optimum reaction temperature*** established, or the influence of water, present in the reaction mixture****, on the yield of aldehyde. Finally, it should be mentioned that the aldimine salt with chlorostannic acid, formed in the reaction, does not always deposit in the precipitate. However, following Stephen's recommendations, in most cases only the precipitate of this salt was hydrolyzed to obtain the aldehyde, without investigating the mother liquor (compare [21]).

In the course of our studies on the synthesis of amino acids labeled with radioactive carbon the need arose to use the Stephen reaction for the preparation of some aliphatic aldehydes from the corresponding nitriles. Since in this case the Stephen method up to now has given only poor results, we were forced to determine on the example of obtaining one of the aliphatic aldehydes (isovaleraldehyde) the optimum conditions for its formation. These conditions were then extended to the synthesis of other aldehydes, namely acetaldehyde and phenylacetaldehyde.

The following was determined as a result of our studies. 1) The aldimine salt with chlorostannic acid, a direct product of reaction, can show variable solubility in the reaction medium. Thus, the phenylacetaldimine salt deposits completely in the precipitate, whereas the acetaldimine salt remains partially in solution, while the

* Communication VII of the series "Investigations of compounds labeled with C^{14} and N^{15}." For previous communications see [1].

** For reviews on the Stephen reactions see [3, 4]; for papers not cited in these reviews see [5-11].

*** For example, Knight and Zook [19] ran the process at 0°, while King and co-workers ran it at the boiling point of ether [12, 13, 20].

**** Slotta and Kethur [18] added water to the reaction mixture, although Stephen recommended running the process in anhydrous ether medium.

isovaleraldimine salt is completely soluble.* For this reason in studying each new case of the Stephen reaction it is necessary to investigate not only the precipitate, separating from the reaction mixture, but also the residue, remaining after evaporation of the solvent.

2) The optimum reaction temperature lies in the limits 15-25°. This data, obtained on the example of reducing isovaleronitrile (see Table 1), also proved valid for both acetonitrile and phenylacetonitrile. Raising the reduction temperature leads to a sharp drop in the yield of aldehyde. The reason for this is cleavage of the diethyl ether by the hydrogen chloride, leading to the formation of alcohol, which converts unreacted nitrile to the imino ester. The formation of the latter was shown in the case of isovaleronitrile by the isolation (after hydrolysis of the reaction mixture) of ethyl isovalerate. If the reduction was run at 100°, then the yield of this ester reached 25%. Small amounts of esters were also shown to be present when isovaleronitrile and phenylacetonitrile were reduced at room temperature (in these cases the esters were converted to the amides for identification). Consequently, concurrently with the reduction of nitriles there is a second process – conversion of the nitriles to imino esters, which can completely suppress the reduction reaction when the temperature is raised.

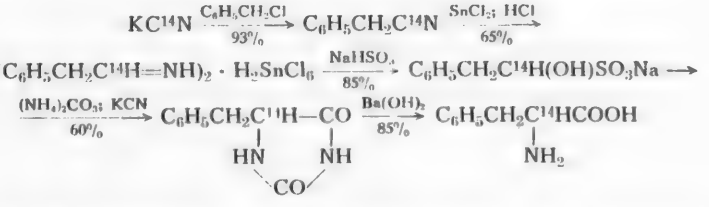
3) The optimum time for the reduction reaction is 7 days. Running the reaction for a longer time does not lead to any material increase in yield, while a shorter reaction time leads to a decrease in yield, which was shown on the example of preparing isovaleraldehyde (see Table 2) and confirmed on the example of phenylacetaldehyde.

4) The optimum amount of stannous chloride in the preparation of isovaleraldehyde is 7 moles per mole of nitrile, while further increase in the $SnCl_2$ is practically without value (see Table 3). However, in the reduction of phenylacetonitrile it proved possible to reduce the amount of $SnCl_2$ to 2.5 moles per mole of nitrile without reducing the yield of aldehyde.

5) The presence of water in the reaction mixture causes the yield of aldehyde to drop, which was shown on the example of reducing isovaleronitrile (see Table 4).

In summary, it was established that under the optimum conditions the yield of isovaleraldehyde is 61-64%; the yield of acetaldehyde under the optimum conditions is 64-67%, and that of phenylacetaldehyde is 55-60% (as the bisulfite compound). Evidently, aliphatic and aralkyl aldehydes are formed in relatively smaller yields than most aromatic aldehydes (compare [3]) for the reason that in preparing the first two types the time required to reduce the nitriles is much longer than in the case of the last type (7 days instead of 5-24 hrs). During this time the hydrogen chloride succeeds in cleaving a substantial amount of diethyl ether with the formation of alcohol, and consequently a substantial amount of imino ester is formed as the result of unreacted nitrile reacting with the alcohol. This circumstance is responsible for a greater reduction in the yield of aliphatic aldehydes when compared to the aromatic aldehydes. For this reason it is in general impossible to use the Stephen method to reduce those nitriles that contain groupings capable of decomposing the intermediate chlorimines (compare, for example, the negative result obtained in the reduction of β-hydroxypropionitrile [14]). It would be desirable in the future to search for such solvents for the Stephen reaction as would be less prone to cleavage by hydrogen chloride than diethyl ether.

The reduction of phenylacetonitrile to phenylacetaldehyde by the Stephen method was used by us to synthesize phenylalanine-2-C^{14}, starting with $KC^{14}N$. The yield of labeled phenylalanine was 25-26%, based on $KC^{14}N$.



* It should be mentioned that the solubility of these salts in water is similar to their solubility in ether, saturated with HCl. Thus, the phenylacetaldimine salt, in contrast to the two other salts, is insoluble in both HCl-saturated ether and water. This circumstance makes hydrolysis of the given salt difficult, and to avoid polymerization of the aldehyde as it is formed it is expedient to convert the aldehyde directly to the bisulfite compound by boiling with bisulfite solution.

Many other amino acids, labeled with C^{14} in the α-position, can be synthesized by a similar procedure. An advantage of the proposed method of synthesizing 2-C^{14}-amino acids is the small number of steps involved, in which respect it differs favorably from all of the earlier described methods of introducing tracer elements in the α-position of amino acids.

EXPERIMENTAL

1. Determination of optimum conditions for preparation of isovaleraldehyde. Anhydrous stannous chloride* and absolute ether, the latter containing not more than 0.01-0.03% water (determined by the K. Fischer method), were placed in a flask. The amount of ether taken was 1 ml per millimole of $SnCl_2$. The flask was attached to a head which was fitted with tubes (with stopcocks) for the admission and escape of gas, and also a dropping funnel. Hydrogen chloride, thoroughly dried by passage through H_2SO_4 and $Mg(ClO_4)_2$, entered the flask through the inlet tube, while the outlet tube was connected to a Tishchenko flask, containing concentrated H_2SO_4. With water cooling, a stream of hydrogen chloride was passed into the mixture until all of the stannous chloride had dissolved and two liquid layers were obtained.** Then either 1.00 ml (9.55 mmoles) of isovaleronitrile or its solution in absolute ether was added through the funnel (using the air pressure of a rubber bulb), the funnel rinsed twice with 1-2 ml of absolute ether, and then hydrogen chloride was again passed into the solution until completely saturated. The reaction mixture was allowed to stand for a certain length of time at the desired temperature, then the ether and hydrogen chloride were removed on the water bath (at the end using a water-jet pump), 100 ml of water was added to the residue, and the mixture was subjected to distillation for 30 min. The aldehyde in the distillate was determined either by the oxime method [24] or gravimetrically as the 2,4-dinitrophenylhydrazone.

TABLE 1

Effect of Reaction Temperature on Yield of Isovaleraldehyde (2 moles of $SnCl_2$ per mole of nitrile)

Reaction time	Temperature	Yield (in %)
7 days	0°	15
7 "	15-25	32
7 "	37	15
3 hrs	100	0

TABLE 2

Effect of Reaction Time on Yield of Isovaleraldehyde (7 moles of $SnCl_2$ per mole of nitrile; temperature 15-25°)

Reaction time (in days)	Yield (in %)
1	31
3	40
5	49
7	61-64
14	65

TABLE 3

Effect of Amount of $SnCl_2$ on Yield of Isovaleraldehyde (Reaction time 7 days; temperature 15-25°)

Number of moles of $SnCl_2$ per mole of nitrile	Yield (in %)
2.0	32
4.0	46
7.0	61-64
9.4	66

TABLE 4

Effect of Amount of Water on Yield of Isovaleraldehyde* (7 moles of $SnCl_2$ per mole of nitrile; reaction time 7 days; temperature 15-25°)

Number of moles of water per mole of nitrile	Yield (in %)
0	61-64
3.6	32-47
7.0	25
14.0	< 5

The data on the influence of temperature, reaction time, amount of stannous chloride and addition of water on the yield of isovaleraldehyde are given in Tables 1-4. The yield of isovaleraldehyde under the

* The water was added as either partial or complete replacement of anhydrous stannous chloride by the dihydrate.

* Stannous chloride was dehydrated by the method of [22] in a vacuum-desiccator over sulfuric acid for a week. The treatment recommended by Stephen [23] of using acetic anhydride to dehydrate stannous chloride dihydrate yields a reducing agent of inferior quality. The attempted recrystallization of anhydrous stannous chloride from pyridine [2] leads to decomposition of the reagent; see also [18].

** The absence of two layers means that water is present in the reaction mixture, which causes the yield of aldehyde to drop; such a solution cannot be used for the reduction.

optimum conditions (15-25°, reaction time 7 days, amount of $SnCl_2$ 7 moles per mole of nitrile) is 61-64%.

2. Preparation of acetaldehyde. The reaction was run using the optimum conditions described in Expt. 1 for the preparation of isovaleraldehyde. A yellow precipitate was obtained as a reaction result, from which we isolated $^7/_8$ of the obtained aldehyde, while the other $^1/_8$ was in the solution. However, it is more expedient not to isolate the precipitate, but instead to treat it together with the solution in the manner described in Expt. 1. The yield of aldehyde was 64-67%.

3. Preparation of phenylacetaldehyde. a) Preparation of phenylacetaldimine salt with chlorostannic acid (for the conditions see Expt. 1). A mixture of 25 ml of absolute ether and 5 g of $SnCl_2$ (2.6 mmoles) was placed in the apparatus flask. The mixture was saturated with hydrogen chloride and then 1.1 ml of benzyl cyanide (9.6 mmoles) was added. After 7 days the precipitate was suction-filtered, washed with absolute ether, and dried in a vacuum-desiccator over either NaOH or H_2SO_4; weight 1.8-2.5 g.*

The salt, prepared for analysis, was suction-filtered in the absence of atmospheric moisture and then washed with absolute ether that had been saturated with hydrogen chloride. The salt was obtained as a white crystalline substance that slowly liberated the aldehyde when kept in the air.

Found %: Sn 20.55, 20.60; N 4.68, 4.73; Cl 37.68, 37.87. $[C_8H_9N]_2 \cdot H_2SnCl_6$. Calculated %: Sn 20.76; N 4.90; Cl 37.21.

b) Preparation of bisulfite compound of phenylacetaldehyde. The aldimine salt (1.3 g) was added to a solution of $NaHSO_3$, obtained by saturating a suspension of 5.8 g of $NaHCO_3$ in 20 ml of water and 2 ml of butanol with SO_2. The mixture was refluxed for 2 hrs (heating in an oil bath), the obtained precipitate was suction-filtered and washed with water, and the filtrate was evaporated to dryness. About 5.8 g of substance was obtained here, containing 13-16% of the phenylacetaldehyde bisulfite compound; the phenylacetaldehyde was determined as the 2,4-dinitrophenylhydrazone (see [26]). If analytically pure aldimine salt was used, the yield of phenylacetaldehyde was 85%. The yield of phenylacetaldehyde, based on the starting nitrile, was usually of the order of 55-60%.

4. Preparation of phenylalanine-2-C^{14}. Radioactive benzyl cyanide (2.1 ml), purified by distillation (for its preparation from benzyl chloride and $KC^{14}N$ see [25]), was reduced by the Stephen method under the conditions of Expt. 3a. The obtained 3.35 g of phenylacetaldimine salt with chlorostannic acid (yield 65%) was converted to the bisulfite compound as described in Expt. 3b. A mixture of 15.1 g of the isolated bisulfite compound (phenylacetaldehyde content 14.7%), 0.98 g of potassium cyanide, 6.5 g of ammonium carbonate, 24 ml of 25% aqueous ammonia and 12 ml of alcohol was heated with constant shaking in a sealed tube at 100° for 1 hr. The obtained 5-benzylhydantoin (weight 1.13 g, yield 60%) was isolated using the conditions described earlier in the synthesis of 1-C^{14}-tyrosine [26]. The hydantoin was heated with constant shaking for 1 hr at 150-160° in a sealed tube with 3 g of $Ba(OH)_2 \cdot 8H_2O$ and 16 ml of water. The precipitate of barium carbonate was suction-filtered, washed with hot water, the filtrate treated with 0.7 g of ammonium carbonate, the precipitate filtered, the filtrate evaporated to dryness, and the phenylalanine-2-C^{14} transferred to a suction-filter funnel using 5-8 ml of alcohol. Yield 0.85 g (86%); m. p. 256-257° (with decomp.).

SUMMARY

1. The conditions for the preparation of aliphatic and aralkyl aldehydes, and specifically of acetaldehyde, isovaleraldehyde and phenylacetaldehyde, by the Stephen reaction were investigated.

2. It was shown that together with reduction of the nitriles to aldimines there is a concurrent transformation of the nitriles to imino esters, proceeding due to reaction with the alcohol formed in the cleavage of diethyl ether with hydrogen chloride. By raising the temperature it is possible for the reduction of the nitrile to be completely suppressed by the latter process.

3. The reduction of benzyl cyanide to phenylacetaldehyde by the Stephen method was utilized to synthesize phenylalanine-2-C^{14}, starting with $KC^{14}N$.

* If the reaction time is reduced to 1-3 days, then the amount of obtained salt remains approximately the same, but the yield at the stage of obtaining the bisulfite compound of the aldehyde shows a sharp drop.

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THE POLYMERIC PEROXIDE OF VINYL CHLORIDE

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As has been noted several times in the literature, vinyl monomers react with oxygen to form peroxide compounds. Polymeric peroxides have been isolated in a series of cases for some vinyl compounds: diphenylethylene [1], α-terpilene [2], styrene [3, 4], indene [5], chloroprene [6], methyl methacrylate [7], vinyl acetate [7], 2,3-dimethylbutadiene [8], acrylonitrile [9], α-methylstyrene [10] and methacrylonitrile [11] and their structures may be expressed by the general formula

$$[-O-(CH_2-\underset{\displaystyle R}{\underset{|}{C}}H)_n-O-]_x,$$

where $n \geq 1$, depending on the nature of the monomer and experimental conditions.

When monomers reacted with oxygen, two types of reactions were noted: the formation of polymeric peroxides and of carbonyl compounds. Hydroperoxide and carbonyl end groups were identified. In addition, cyclic $\left(-\underset{\displaystyle O-O}{\underset{|}{C}}-\underset{|}{C}-R\right)$ or epoxide $\left(-\underset{\displaystyle O}{\underset{/\backslash}{C}}-C-R\right)$ structures were proposed for the end groups [3].

In a series of cases, the decomposition products of polyperoxides of vinyl compounds were determined. In most cases the decomposition occurred in such a way that the break in the peroxide (−O−O−) bonds was accompanied by rupture of the adjacent (−C−C−) bonds to form a mixture of formaldehyde and the carbonyl compound corresponding to the given monomer; the polymeric peroxide of styrene decomposed to formaldehyde and benzaldehyde; methacrylonitrile polyperoxide – to formaldehyde and pyruvonitrile; methyl methacrylate polyperoxide – to formaldehyde and methyl pyruvate; diphenylethylene polyperoxide – to formaldehyde and diphenyl ketone, etc.

The peroxides of chlorovinyl compounds have hardly been studied. Reinhardt [12] described vinylidene chloride peroxide, whose structure was not established accurately. This peroxide was formed by the action of atmospheric oxygen on vinylidene chloride at −40° and +25° and could initiate the polymerization of this monomer. The peroxide itself was readily exploded by heating or by a slight mechanical blow. Slow decomposition of vinylidene chloride peroxide gave formaldehyde, phosgene and hydrogen chloride. The peroxide compounds of vinyl chloride were not investigated. It is only known that the existence of an induction period during the polymerization of this monomer is explained by the monomer reacting with oxygen [13]. We could not find any more detailed data on chlorovinyl peroxide compounds.

We showed [14] that in polymerizing vinyl chloride in the presence of air, at first only peroxide compounds were formed until the complete disappearance of oxygen from the gas phase.

The aim of the present work was to isolate peroxide compounds of vinyl chloride and to establish their structures. In addition, as oxygen is almost always found in greater or smaller amounts in the polymerization of vinyl chloride in production reactors, it seemed interesting to study the properties and reactivity of the polymeric peroxide and to elucidate its effect on the quality and properties of the polymer produced.

During the induction period in the mass polymerization of vinyl chloride in the presence of molecular oxygen, a yellowish viscous liquid was obtained which vigorously liberated iodine from an acetic acid solution of

potassium iodide. It decomposed with an explosion when brought near a naked flame and also when ground with a glass rod under water. In the latter case characteristic crackles from explosions could be heard.

Due to the instability of the compounds being investigated and the difficulty of obtaining sufficiently large amounts (all the operations were carried out with several tens of milligrams, prepared for each experiment separately) reprecipitated vinyl chloride peroxide could not be isolated. As a result of these circumstances, the quantitative determinations could be low in comparison with the calculated ones.

One could assume that on oxidizing vinyl chloride, the polymeric peroxide is formed by the copolymerization of vinyl chloride and oxygen. This hypothesis was confirmed by the determination of peroxide compounds formed at 50° during the induction period in 1 g of vinyl chloride, containing 0.5% by weight of azoisobutyrodinitrile as an indicator, as these results showed [14] that the amount of peroxide compounds of this monomer in the reaction mixture increased up to the moment when this monomer started precipitating at a constant rate, equivalent to 0.073 ml of $Na_2S_2O_3$/hr. The first order decomposition constant of the azoisobutyrodinitrile at this temperature was 0.0107 hr^{-1} [15]. It follows from this that if every radical formed participated in the chain growth reaction, then in an hour a peroxypolymer would be formed with an average degree of polymerization of P = 6-7. Actually, the value may be somewhat higher as some of the radicals are used up in side reactions [16].

The formula of the ideal 1:1 copolymer of oxygen and vinyl chloride should be

$$\left[-O-CH_2-\underset{\displaystyle Cl}{\underset{|}{CH}}-O-\right]_n.$$

As can be calculated readily, a sample of polyperoxide should contain 33.86% of oxygen and 37.59% chlorine. The ratio $\frac{\%O}{\%Cl} = 0.903$.

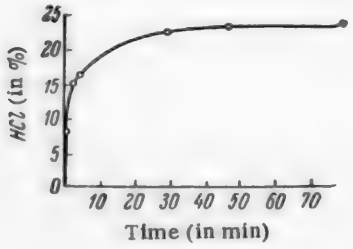


Fig. 1. HCl evolution kinetics during hydrolysis of the polyperoxide with water.

The average oxygen content determined iodometrically from a whole series of experiments was 26.7% (26.0-27.8%), which is less than that calculated. Determination of HCl after hydrolysis of the peroxide with water at 60-70° also gave a low chlorine content – 29.3%. The ratio $\frac{\%O}{\%Cl} = 0.911$.

As the polymeric peroxide of vinyl chloride was not purified or recrystallized, one may assume that considering the very close values of $\frac{\%O}{\%Cl}$, the given compounds had, in all probability, a 1:1 structure with regular sequences of the units ($-CH_2CHClOO-$).

The infrared spectrum of the vinyl chloride peroxide in a carbon tetrachloride solution had an intense, wide absorption band at 883 cm^{-1}, which is characteristic of peroxide compounds and due to the $-O-O-$ bond, and a strong absorption band at 1080 cm^{-1}, which could have been due to the presence of the $-\underset{|}{\overset{|}{C}}-O-O-$ group [17]. The presence of hydroperoxide groups was not shown clearly. It was shown [17] that this group forms the following bands in an IR spectrum: 840 cm^{-1} (O–O–H), 880 cm^{-1} (O–O), 3450 cm^{-1} (O–H) and 6800 cm^{-1} (1st overtone of O–H bond).

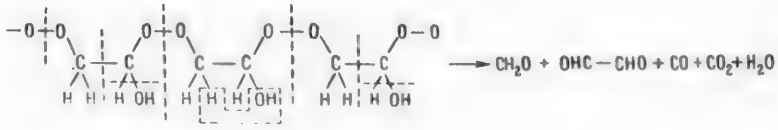
The peroxide being investigated had no bands at 3450 and 6800 cm^{-1} and the band at 817 cm^{-1}, which could probably be explained by $-O-O-H$ group vibrations, was extremely weak. There was also no absorption band in the region of 1170 cm^{-1}, which is assigned to the ether group $-\underset{|}{\overset{|}{C}}-O-\underset{|}{\overset{|}{C}}-$ [18].

The exceptional lability of the chlorine atom in the polyperoxide of vinyl chloride should be noted. Even during hydrolysis in the cold, the chlorine was eliminated from the polymeric molecule at a high rate (Fig. 1). This is not surprising as the capacity of α-chloro substituted ethers for hydrolysis by water is well known. It follows from this that molecular oxygen is not only an inhibitor of vinyl chloride polymerization, but also, due to the

rapid hydrolysis of polymeric peroxides, formed during the polymerization induction period, it lowers the pH of the reaction medium. This has a negative effect on the optimal conditions for the decomposition of initiators, the yield and properties of the polymer and strongly affects conjugated solution [19], which is important not only for emulsion but also bead polymerization.

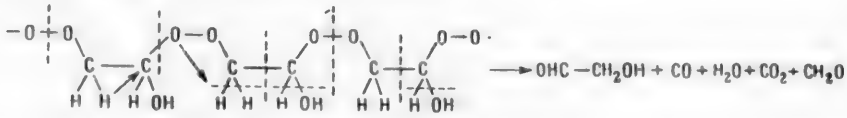
The polyperoxide of vinyl chloride reacted with water even in the cold to split out a chlorine ion quantitatively to form HCl; at a higher temperature (50°) it decomposed. Among the products were found HCl, formaldehyde, glyoxal, CO and CO_2. In accordance with this, the polymeric peroxide of vinyl chloride is decomposed by water in two stages:

(1)



(2)

It should be noted that glyoxal $(CHO)_2$ was identified by the formation of the osazone by 2,4-dinitrophenylhydrazine. However, exactly the same osazone may be formed by glycoaldehyde, which could also be a possible decomposition product of vinyl chloride polymeric peroxide



(3)

Decomposition by this equation gives carbon monoxide, hydrogen chloride and glycolaldehyde. Carbon monoxide in this case may be formed by the peroxide oxygen atom attacking a formaldehyde molecule, apparently at the moment of decomposition.

Data in the work of Strause and Dyer [11] on the oxidation of methacrylonitrile, supports such a hypothesis. They considered that carbon monoxide and dioxide, produced in the decomposition of polymeric methacrylonitrile peroxide, were formed as a result of formaldehyde oxidation and this was intensified by ultraviolet radiation.

A balance of the decomposition products may be used to decide between the two possible decomposition schemes, (2) and (3) (see Table 1). If we consider decomposition by Eq. (2) only, we do not find a considerable amount of the products (~ 15%); however, calculating by Eq. (3), we find, on the contrary, an excess of them (~ 10%). Taking into account the possible inaccuracies in the determination, it is difficult to decide on the possibility of decomposition by one or other scheme due to the small amounts of material analyzed.

As CO_2 was formed from the end groups, independent of decomposition schemes (2) or (3), if one tentatively assumes that the number of CO_2 molecules corresponds to the number of polymeric peroxide molecules and that the number of HCl molecules corresponds to the number of $(-CH_2CHClOO-)$ units in the chain, then in various experiments the ratio $\frac{HCl}{CO_2}$ = 17-26, which gives an average molecular weight of 1600-2500.

Experiments on the initiation of the polymerization of various monomers by vinyl chloride polymeric peroxide showed that it induced polymerization of styrene, vinylidene chloride, vinyl chlorine, butyl methacrylate and methacrylic acid.

It was noted in many works in which the polymerization capacity of polyperoxides was studied, that the process was due to radicals, formed during the decomposition of polymeric peroxides [11, 20]. This conclusion does not always agree with experimental material as such a decomposition would have led to a sharp increase in the rate of polymerization and to an ever increasing capacity of the monomer for absorbing oxygen from the gas phase. Actually, the amount of peroxide compounds grows linearly with time [14]. Some data show that after the

induction period in vinyl chloride polymerization, there is a slight increase in the rate of the true polymerization.

Miller and Mayo [3] found that the increase in the rate of formation of polymeric styrene peroxide in the presence of 0.01 M of polyperoxide was by a factor of only 1.7, while an equal amount of azoisobutyrodinitrile increased the rate of polyperoxide formation by a factor of 55.

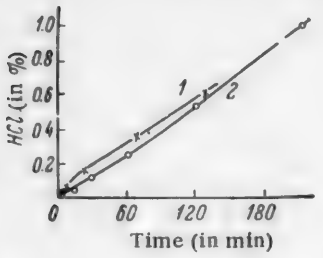


Fig. 2. Kinetics of HCl evolution in the thermal decomposition of polyvinyl chloride. 1) Obtained during polymerization initiated by polymeric peroxide (decomp. at 72°), 2) industrial (decomp. at 161.5°).

In all probability polymeric peroxides are not only capable of splitting by a free radical mechanism and then initiating true polymerization, but also act as stable radicals $R(MO_2)_x\cdot$ with an extended life time. The existence of such a radical was confirmed by the capacity of a polymeric peroxide solution in a monomer to decolorize a solution of diphenylpicrylhydrazyl in dichloroethane [21]. It follows from this that the hydroperoxide and carbonyl groups identified in certain polymeric peroxides and the hypothetical epoxy and cyclic end groups may not be the only possible ones. Actually, the IR spectrum of vinyl chloride polymeric peroxide did not show the presence of the $-O-O-H$ group clearly. However, the absorption bands characteristic of carbonyl groups (1725 cm^{-1}) [17] and epoxy groups (1170 cm^{-1}) [18] were not found. It should also be noted that paper [22] examined the polymerization of styrene in the presence of air. The changes in magnetic susceptibility showed that the radicals were stabilized by the action of oxygen and that their concentration in the reaction mixture increased. This observation agrees with our hypotheses.

The radical with structure $R(MO_2)_x\cdot$ is capable of opening a double bond to form radicals of the type $R(MO_2)_xM_y$. This radical should possess almost all the properties of a normal polymeric radical of the type $RM\cdot_z$ and in the absence of molecular oxygen it should start to grow with the monomer. In this case, naturally, a polymer with the structure $R(MO_2)_xM_y\cdot$ or $R(MO_2)_xM_y(MO_2)_kR$ should be formed. The latter may be formed by the recombination of radicals of type $R(MO_2)_xM_y\cdot$ with polyperoxide radicals. Such a hypothesis was confirmed by investigating a polymer, obtained during the polymerization of vinyl chloride, initiated by its own polymeric peroxide. The preparation was first carefully washed with liquid vinyl chloride till it was completely freed from free peroxide and then washed three times with methanol. The polymer analyzed had a low chlorine content (54.44%), a low molecular weight (some samples had a molecular weight of 20,000-30,000) and an exceptionally low decomposition point (< 70-80°), which for a normal polyvinyl chloride resin is of the order of 150°. Such a low decomposition point may be explained by the early breakdown of the polyperoxide ring of a polymeric molecule of the type $R(MO_2)_xM_y$. We plotted the kinetics of resin decomposition at 175° by the evolution of HCl, using an electroconductivity method. Figure 2 illustrates a typical experiment. It also shows the relation of HCl evolution to time for a resin obtained industrially and this appears as a straight or almost straight line with a certain tendency towards an increase in the elimination of HCl during the experiment. The line for the resin investigated shows a definite change of slope. HCl was evolved more rapidly in the first few minutes of the experiment which, apparently, was due to decomposition of the peroxide part $R(MO_2)_x$ of the polymer molecule. Then, after the change in slope, the rate of hydrogen chloride evolution, which apparently characterized the decomposition of the true polymer, M_y, continued at a much slower rate. The products of polymer decomposition by water at a high temperature were analyzed and the peroxide oxygen content determined in 1 g sample of the resin, in which was found HCl 0.0000347 mole, O_2 – 0.0000365 mole and > CO 0.0000713 mole.

The amount of hydrogen chloride (0.13%) found in the polymer by this method practically coincided with the amount of HCl evolved by the polymer up to the moment when the rate of the thermal decomposition of the resin changed (Fig. 2, curve 1).

We concluded from the data obtained from investigating the properties of polyvinyl chloride, prepared by initiation of vinyl chloride with polymeric peroxide, that an unusual block polymer was produced, one part of which had a polyperoxide structure and the other the structure of a true polymer.

Thus, in vinyl chloride polymerization, molecular oxygen, besides having a strong inhibiting effect, also negatively affects the quality of the polymer obtained, by greatly lowering the decomposition point, the molecular weight and some other properties of the resin.

EXPERIMENTAL

The polymeric peroxides were prepared in sealed ampules of 70-80 ml capacity from 3-5 g of vinyl chloride and air in the gas phase at 45-50° with continuous agitation in a vibrating thermostat. After 8-10 hrs the ampules were removed and those which did not contain traces of polymer were opened. Their contents were transferred to a tared flask, filled with nitrogen and placed in a bath of snow, and the monomer distilled off. The flask was reweighed to determine the weight of the peroxide.

In some experiments, a very small amount of azoisobutyrodinitrile was added for determining the rate of polymeric peroxide formation.

The peroxide oxygen was determined by the usual iodometric method. Into the flask, containing the sample of peroxide, was introduced 3.5 ml of glacial acetic acid (chemically pure) and 11 ml of 5% potassium iodide in methanol. The methanol was first treated with active charcoal and then distilled twice.

The mixture was kept in the dark and the iodine liberated was titrated with 0.1 N hyposulfite solution.

Hydrolysis of vinyl chloride polymeric peroxide. The flask, containing the sample of peroxide examined (0.3-0.5 g), was placed on a water bath maintained at 50-60°. The gases liberated were passed through a small reflux condenser and collected in a Hempel burette and analyzed. The CO and CO_2 were found.

HCl and a mixture of aldehydes were identified in the aqueous phase. The aldehydes were isolated as the 2,4-dinitrophenylhydrazones, which were separated by paper chromatography [23] on acetylated paper [24].

A series of experiments established that we had at least two compounds to deal with. Identification of the components from the relative movements of the concentration maxima of the substances, $R_f = a/b$ (where a is the movement of the concentration maximum of the substance in centimeters and b is the movement of the solvent

TABLE 1

Composition of Decomposition Products of Polymeric Peroxide of Vinyl Chloride

Sample of polyperoxide (g)		0.3470	0.4200	0.4002
Found	CO	32.4 ml	39.6 ml	38.1 ml
		0.0406 g	0.0495 g	0.0477 g
	CO_2	2.8 ml	5.2 ml	2.9 ml
		0.0052 g	0.0102 g	0.0057 g
	$-\overset{\overset{O}{\|\|}}{C}-$ groups (g)	0.0555	0.0980	0.0835
	HCl (g)	0.089	0.1463	0.1210
Amount of polyperoxide, relative to HCl, considering a 1 : 1 structure (g)		0.230	0.378	0.313
Molecular weight of polymeric peroxide (from CO_2)		1740	1640	2420
Amount of formaldehyde (in g), contained in decomposition products of the polyperoxide, calc. by scheme (2)		0.0435	0.0530	0.0511
Amount of glyoxal (in g), contained in the polyperoxide decomposition products, calc. by scheme (2)		0.0209	0.0458	0.0370
Balance of polyperoxide decomposition products, calc. by scheme (2)		0.1991	0.3048	0.2625
Amount of glycoaldehyde (in g), contained in polyperoxide decomposition products, calc. by scheme (3)		0.1300	0.2100	0.1790
Balance of polymeric peroxide decomposition products (in g), calc. by scheme (3).		0.2647	0.4160	0.3534

front), showed the presence of formaldehyde hydrazone and the osazone of an unknown compound in the mixture. The osazone spot gave a blue color when treated with alcoholic alkali in contrast to the hydrazone, which gave a blood red color. For formaldehyde we found R_f 0.37-0.39, while according to [21] the R_f is 0.38. The R_f of a reference spot was within these limits.

Using the different solubilities in alcohol, we washed out the osazone from the hydrazone by washing the mixture several times with alcohol.

From analysis data and melting point, the compound corresponded to the osazone of glyoxal. The m. p. was 306-309° and according to [25] it should be 311°.

Found %: C 39.20; N 25.80; H 2.49. $C_{14}H_{10}O_8N_8$. Calculated %: C 40.19; N 26.70; H 2.41.

The formation of formaldehyde was also confirmed by formation of the dimedone derivative [26] with m. p. 185°; a mixed sample melted at 185-185.5°.

Data from three experiments in which the decomposition products of the polymeric peroxide were determined quantitatively are given in Table 1.

The preparation of polymer using vinyl chloride polymeric peroxide was carried out by heating solutions of vinyl chloride polyperoxide in the appropriate monomer at 50° in sealed ampules in an atmosphere of nitrogen. Blank experiments were run in parallel. The ampules were filled with monomer and opened on a special apparatus [27].

In all cases, polymers were obtained. Vinyl chloride polymeric peroxide in concentrations of about 0.1 M produced polymerization of styrene after 20 hrs, of vinylidene chloride after 4 hrs, of butyl methacrylate after 20 hrs and of methacrylic acid after 15 hrs.

TABLE 2

Wavelength (μ)	Frequency (cm^{-1})	Intensity value	Group
12.35	817	Very weak	O–O–H
11.35	883	Broad	O–O
9.25	1080	Strong	C–O–O
7.55	1323	Average	
7.53	1330	Average	CH (deformation)
7.50	1333	Average	
6.20	1618	Weak	C–C
3.55	2810	Average	CH (bond)
3.40	2920	Average	

Decomposition of polymer with water. To a sample of the resin, weighing 1 g, was added 50 ml of water, after which the mixture was heated for 1 hr on a water bath at 80-90°. The aqueous phase was analyzed for HCl and CO groups. The HCl was determined by titration with 0.01 N alkali and the carbonyl groups by reaction with hydroxylamine hydrochloride.

Determination of the HCl evolution kinetics during thermal decomposition of the polymer obtained during the polymerization of vinyl chloride, initiated by the polymeric peroxide, was carried out by measuring the electroconductivity using the method described in [28]. 0.4 g of polyvinyl chloride was introduced into a vessel, which was placed in a thermostat at 175° ± 0.01. Then purified air and dried air was passed through the system at a constant rate of 0.3 liters/min. The hydrogen chloride, flushed out by the air, passed into a thermostated vessel, containing a known amount of distilled water, where the HCl was absorbed completely. After given time intervals, the electroconductivity of the HCl solution was measured.

Determination of the HCl evolution kinetics, during the decomposition of the polymeric peroxide with water (Fig. 1), was carried out by measuring the electroconductivity by a procedure similar to that described above.

The difference was that the sample of peroxide was introduced directly into the thermostated vessel, which was then charged with a determined amount of distilled water with a known electroconductivity.

Data of spectroscopic investigation.* The infrared spectrum of a solution of the polymeric peroxide in carbon tetrachloride is given in Table 2.

SUMMARY

1. The polymeric peroxide of vinyl chloride was isolated. Its properties and hydrolysis and initiation capacities were investigated.

2. The polymer obtained by initiating the polymerization of vinyl chloride with the polymeric peroxide, had a low decomposition point and a lower molecular weight than the polymer prepared with the normal initiators. A structure was proposed for this polymer.

3. A decrease in the pH of the reaction medium in suspension polymerization of vinyl chloride may be caused by the presence of molecular oxygen from the hydrolysis of polymeric peroxides, formed during the induction period.

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REACTION OF AROMATIC COMPOUNDS WITH ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

IV. REACTION OF BENZENE WITH POLYHYDRIC ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

I. P. Losev and O. V. Smirnova

In previous investigations on the reaction of benzene with alcohols in the presence of acid catalysts, we confirmed the hypothesis that primary alcohols are difficult to condense with benzene; this reaction proceeds much more readily with secondary and tertiary alcohols.

A study of the reaction of benzene with various polyhydric alcohols in the presence of acid catalysts is interesting as a possible means of preparing new saturated and unsaturated benzene derivatives (phenylpropanols, phenylbutylene, etc.) suitable for the synthesis of plasticizers and polymeric compounds.

We based our procedure for reacting benzene with diols on data from the investigations of various authors, published in the literature [1-8]. We first condensed benzene with butanediol-1,4 in the presence of H_3PO_4 and $AlCl_3$. However, under these conditions, no individual products could be isolated besides tarlike reaction products which were readily soluble in the normal organic solvents. Therefore, further investigations were carried out with butanediol-1,3. In this case the formation of two substances was possible: the reaction product of benzene 1) with the secondary alcohol group, 3-phenylbutanol-1 (I) and 2) with both alcohol groups, 1,3-diphenylbutane (II). In fact, both these substances were obtained and characterized, with 3-phenylbutanol-1 as the main product (up to 45.4% yield).

The dehydration of (I) was a separate problem, as it is known from the literature [9, 10] that lengthening the radical of a particular alcohol makes its dehydration more difficult. The dehydration was carried out under the conditions recommended for the dehydration of primary phenylethyl alcohol [9, 11, 12]. As catalysts we used H_2SO_4, NaOH, grade "M" cation-exchange, tar adsorbent, silica gel, alumina gel and aluminosilica gel. The best yield of 2-phenylbutene-3 (III) (56%) was obtained in the presence of aluminosilica gel at 140-160°. Under these conditions the catalyst may be regenerated completely.

On the basis of literature data [13-16] one could assume that the olefin we prepared would polymerize much more slowly than styrene and α-methylstyrene. Actually, none of the attempts to polymerize (III) in a pure form in the presence of benzoyl peroxide, $AlCl_3$ and BF_3 gave positive results. Therefore, we then used copolymerization of (III) with styrene. For this we tested various component ratios. Polymerization was carried out by heating to 60-70°. The addition of 1, 5 and 10% of (III) to styrene very slightly retarded the polymerization of the latter.

We then investigated the condensation of benzene with glycerol in the presence of H_3PO_4, $AlCl_3$, $FeCl_3$, H_2SO_4. Positive results were obtained in the presence of $AlCl_3$, at 100-102° and 5.5-6.0 atmos in an autoclave. The reaction gave two products: 2-phenylpropanediol-1,3 (IV) and 2,3-diphenylpropanol-1 (V).

EXPERIMENTAL

a) Condensation of benzene with butanediol-1,3 in the presence of $AlCl_3$. The reaction mixture consisted of 234.0 g (3 moles) of benzene, 90.0 g (1 mole) of butanediol-1,3 and 266.0 g (2 moles) of $AlCl_3$. The mixture was heated in a flask with a reflux condenser at 92-93°. The reaction was continued until the evolution of HCl ceased. The mixture was then poured into cold water and the product separated from the aqueous acid layer,

washed until neutral, dried and distilled at 1-3 mm. From the distillation we obtained 4 fractions.

The 1st fraction was a mixture of the starting butanediol-1,3 and reaction products.

The 2nd fraction was redistilled to give a product with b. p. 120-122° at 22 mm (236-238° at atmospheric pressure), which corresponded to 3-phenylbutanol-1 (I). The yield was 45.4%.

d^{20}_4 0.9821, $n^{20}D$ 1.5160, MR_D 49.7; calculated 49.3. Found %: C 80.35, 80.40; H 9.6, 9.76; OH 11.21. M 148.4. $C_{10}H_{14}O$. Calculated %: C 80.00; H 9.33; OH 11.3. M 150.0.

To establish the structure of (I), it was oxidized in acetic acid with potassium bichromate. For the reaction we used 4.0 g of (I), 65 ml of acetic acid, 8.6 g of potassium bichromate and 8.5 ml of water. The reaction was performed at 80-90°. From the oxidation we obtained a product with b. p. 115° at 2 mm (223-225° at atmospheric pressure) in 25% yield and this was 3-phenylbutyraldehyde.

Found %: C 81.24, 81.47; H 8.51, 8.62. M 148.8. $C_{10}H_{12}O$. Calculated %: C 81.08; H 8.10. M 148.0.

The presence of an aldehyde group was confirmed by qualitative reactions.

On standing in air, the 3-phenylbutyraldehyde was converted into a white crystalline substance with m. p. 37-38°, which corresponded to 3-phenylbutyric acid.

The 3rd fraction was redistilled to give a product with b. p. 196-198° at 2 mm (298-300° at atmospheric pressure).

d^{20}_4 0.991, $n^{20}D$ 1.5217. Found %: C 91.84, 91.28; H 8.61, 8.48. M 208.5. $C_{16}H_{18}$. Calculated %: C 91.43. H 8.57; M 210.0.

These data correspond to 1,3-diphenylbutane (II). To establish the structure of (II), it was oxidized with potassium bichromate in acetic acid at 80-90°. We used 2.6 g of 1,3-diphenylbutane, 8.6 g of potassium bichromate, 8.5 ml of water and 55 ml of acetic acid. Distillation of the oxidation products yielded a substance with b. p. 202°, which gave a positive reaction for acetophenone, and a substance with b. p. 268-270° and m. p. 76° (from benzene). The latter did not depress the melting point of phenylacetic acid.

The 4th fraction was a dark red, tarry mass, which solidified in air.

b) Dehydration of 3-phenylbutanol-1 in the presence of aluminosilica gel. We used 10.0 g of 3-phenylbutanol-1 and 20.0 g of sodium hydroxide. The reaction was performed in a copper flask. Water and the dehydration product began to distill off at 140°. After separation of the aqueous layer, the dehydration product was dried with baked copper sulfate, vacuum distilled, then dried with metallic sodium and redistilled in vacuum. We obtained a substance with b. p. 53-55° at 2 mm.

d^{20}_4 0.8805, $n^{20}D$ 1.5042, MR_D 44.41; calculated 44.31. Found %: C 89.59, 89.91; H 10.11, 9.89. Bromine number 119.0. M 129.8. $C_{10}H_{12}$. Calculated %: C 90.90; H 9.09. M 132.0.

The data corresponds to 2-phenylbutene-3 (III), which is not described in the literature and was characterized by us for the first time.

Polymerization of (III) in the pure form did not lead to positive results. Copolymerization of (III) with styrene in the presence of benzoyl peroxide (0.5%) at 70° for 15 hrs gave copolymers with 1.5 and 10% 2-phenylbutene-3 contents.

c) Reaction of benzene with glycerol in the presence of $AlCl_3$. The reaction mixture consisted of 62.0 g of glycerol, 156.0 g of benzene and 66.7 g of $AlCl_3$. The reaction was performed by heating the mixture up to 60° over 15 hrs. Two substances were isolated from the mixture of reaction products by distillation.

1) 2-Phenylpropanediol-1,3 (IV) appeared as an orange-red liquid with b. p. 130-132° at 5 mm.

d^{20}_4 1.1161, $n^{20}D$ 1.5863, MR_D 43.4; calculated 43.16. Found %: C 71.12, 71.31; H 7.89, 7.98; OH 23.11. M 153.4. $C_9H_{10}(OH)_2$. Calculated %: C 71.06; H 7.93; OH 22.37. M 152.0.

2) 2,3-Diphenylpropanol-1 (V) appeared as a red liquid with b. p. 163-166° at 5 mm.

d^{20}_4 1.2147; $n^{20}D$ 1.6151, MR_D 65.2; calculated 65.8. Found %: C 84.02, 84.18; H 7.72, 7.78; OH 7.8. M 214.1. $C_{15}H_{15}(OH)$. Calculated %: C 84.90; H 7.55; OH 8.02. M 212.0.

The products obtained were readily soluble in alcohol, ether, benzene and acetone.

SUMMARY

1. The reactions of benzene with butanediol-1,4 and -1,3 were studied in the presence of phosphoric acid and aluminum chloride.

It was established that benzene reacted with butanediol-1,4 to form tarry products, and with butanediol-1,3 to give 3-phenylbutanol-1 and 1,3-diphenylbutane.

2. Dehydration of 3-phenylbutanol-1 in the presence of aluminosilica gel gave 2-phenylbutene-3.

3. Copolymerization of 2-phenylbutene-3 with styrene gave copolymers with various ratios of the starting components.

4. The reaction of benzene with glycerol in the presence of $AlCl_3$ was studied. This reaction gave 2-phenylpropanediol-1,3 and 2,3-diphenylpropanol-1, which were characterized.

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REACTION OF AROMATIC COMPOUNDS WITH ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

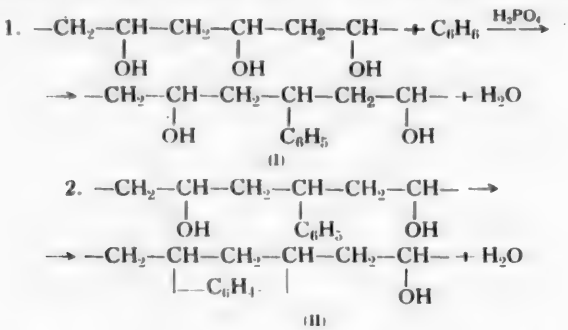
V. REACTION OF BENZENE WITH POLYVINYL ALCOHOL IN THE PRESENCE OF ACID CATALYSTS

I. P. Losev and O. V. Smirnova

In condensing benzene with cellulose [1], it was established that cellulose, dissolved in concentrated sulfuric acid, reacts with benzene and its homologs in the cold with considerable heat evolution; under these conditions three cellulose hydroxyl groups were substituted by aromatic radicals. There is no other data in the literature on the condensation of polyhydric alcohols with benzene.

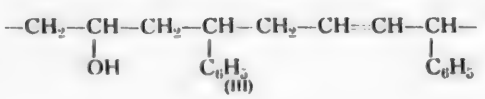
We condensed benzene with polyvinyl alcohol using H_3PO_4 and $AlCl_3$ as catalysts. As a result a red-orange product was obtained, which swelled in water, alcohol, benzene and acetone. Oxidation of the reaction product with potassium bichromate gave phthalic anhydride and benzoic acid, which indicated the inclusion of phenyl rings in the polyvinyl alcohol chain.

The analysis data indicated that the reaction proceeded by the following scheme



The number of hydroxyl groups, substituted by a phenyl ring, depended on the amount of catalyst and duration of the reaction. With all other reaction conditions equal, from 10 to 18% of the hydroxyl groups were substituted by phenyl radicals when the reaction time was varied from 7 to 14 hrs.

The products of reacting polyvinyl alcohol with benzene in the presence of $AlCl_3$ were examined by infrared spectroscopy using a 0.01 mm layer of the substance investigated [2, 3]. The analysis data established that the hydroxyl groups in the polyvinyl alcohol chain are partially substituted by phenyl radicals and as a result the polymer may acquire structure (I) and (II). The formation of double bonds is also possible at the same time and as a result the polymer may acquire structure (III).



The presence of a double bond (III) could result in the formation of cross-links between the separate polymer molecules and this was confirmed by a decrease in the product's solubility after the reaction.

EXPERIMENTAL

1. Reaction of benzene with polyvinyl alcohol in the presence of H_3PO_4. The reaction mixture consisted of 22.0 g (0.5 mole) of polyvinyl alcohol, 117.0 g (1.5 mole) of benzene and from 12.7 g (0.1 mole) to 95.0 g (0.75 mole) of phosphoric acid (d 1.6, 77%).

The reaction was performed in a three-necked flask, fitted with a funnel, a Dean and Stark trap, a reflux condenser, a mercury seal and a paddle stirrer, which was heated to 80-82°. At the end of the reaction, the product was washed with hot water and dried at 50-60°. The results of the experiments are given in Table 1.

TABLE 1

Expt. no.	Amount of H_3PO_4 (in moles)	Duration of reaction (in hrs)	Hydroxyl group content* (in %)	Product yield (in %)	Remarks
1	0.10	7	30.1	5.8	Swelled in water, alcohols, and benzene
2	0.25	10	29.0	17.4	
3	0.25	14	27.3	28.0	
4	0.50	16	26.3	40.0	
5	0.75	10	33.5	—	Dissolved in water

* With a 34% hydroxyl group content of the original polyvinyl alcohol.

To establish the structure of the reaction product, the latter was oxidized with potassium bichromate in an acetic acid medium. 7.0 g of the product was introduced into a three-necked flask, fitted with a stirrer and a reflux condenser, and the oxidizing mixture was added (16.0 g of $K_2Cr_2O_7$, 30 ml of CH_3COOH and 18 ml of H_2O). The oxidation was performed at 60-70° until complete solution occurred (5-6 hrs). After the reaction, the liquid reaction products, boiling in the range 43-59° at 5 mm, were distilled off from the reaction mixture. By sublimation the solid residue yielded a white substance, which formed needle-like crystals with m. p. 131-132° and b. p. 284-286°; they did not depress the melting point of phthalic anhydride.

The analysis data corresponded to phthalic anhydride and after removal of the phthalic anhydride, the reaction product was extracted with benzene in the hot. The benzene extract yielded crystals of benzoic acid (analysis and mixed melting point).

2. Reaction of benzene with polyvinyl alcohol in the presence of $AlCl_3$. The reaction mixture consisted of 22.0 g (0.5 mole) of polyvinyl alcohol, 117.0 g (1.5 mole) of benzene and from 33.3 g (0.25 mole) to 133.3 g (1.0 mole) of $AlCl_3$.

TABLE 2

Expt. no.	Amount of $AlCl_3$ (in moles)	Product yield (in %)	Remarks
1	0.25	6.7	Soluble in organic solvents
2	0.50	14.4	
3	0.75	23.6	
4	0.75	25.3	
5	1.00	26.7	

TABLE 3

Expt. no.	Duration of reaction (in hrs)	Product yield (in %)
1	6	18.0
2	12	28.6
3	18	29.0
4	24	50.6
5	25	51.0

The reaction was carried out under conditions similar to those of the previous experiments at 80-90° for 24 hrs. From the reaction we obtained two products, a liquid and a solid, which were then studied separately. The results of the experiments are given in Table 2.

The dependence of the product yield on the duration of the reaction is shown in Table 3 (benzene 1.5 mole, polyvinyl alcohol 0.5 mole and $AlCl_3$ 0.75 mole).

Liquid reaction product. Distillation yielded a fraction with b. p. 80-82° at 2 mm, corresponding to 1,3-diphenylpentane.

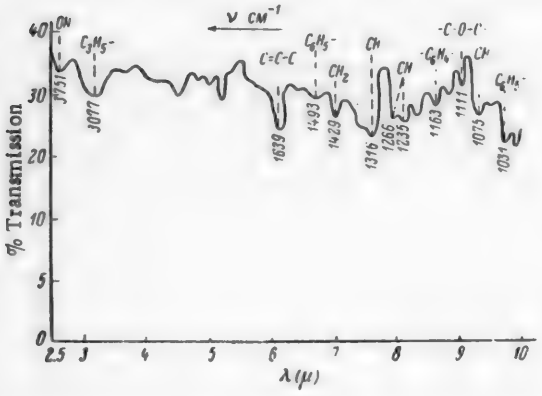
d^{20}_4 1.0318, $n^{20}D$ 1.6008, MR_D 73.2; calculated 73.8. Found %: C 90.86, 91.05; H 8.53, 8.73. M 226. $C_{17}H_{20}$. Calculated %: C 91.07; H 8.93. M 224.

Solid reaction product. After the separation of the benzene layer and the extraction of the acid and water-soluble products, the substance was separated into three fractions by successive precipitations with methyl alcohol. The results of the investigations are given in Table 4.

TABLE 4

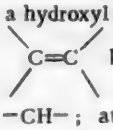
Fraction no.	Hydroxyl group content (in %)	Specific viscosity	Yield (in %)	Remarks
1	32.0	0.2571	13.70	Soluble in water
2	31.0	0.2790	5.20	Soluble in water on heating
3	29.0	0.3834	3.75	Soluble in water on prolonged heating
Original polyvinyl alcohol	34.0	0.2125		

The 3rd fraction was examined further by infrared spectroscopy. The data are given in the figure.



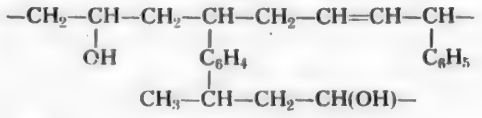
Infrared absorption spectrum of the product from the reaction of polyvinyl alcohol with benzene in the presence of $AlCl_3$.

Bands found: at 3.25 μ (3077 cm^{-1}), 6.7 μ (1493 cm^{-1}), 8.6 μ (1163 cm^{-1}), 9.7 μ (1031 cm^{-1}), corresponding to the phenyl ring; at 2.65 μ (3751 cm^{-1}) – a hydroxyl group; at 6.1 μ (1639 cm^{-1}) – the



bond; at 7.6 μ (13.16 cm^{-1}) – the group $-CH-$; at 7.0 μ (1429 cm^{-1}) – the $-CH_2-$ group and no definite indications of the presence of the CH_3- group.

On the basis of the analysis data and the increased specific viscosity of the solid product from the condensation of polyvinyl alcohol with benzene in the presence of $AlCl_3$, we may consider the condensation product as having the approximate formula



SUMMARY

1. The reaction of benzene with polyvinyl alcohol in the presence of phosphoric acid was investigated. It was established that the reaction gave arylated products. The number of phenyl groups introduced depended on the duration of the reaction and the amount of catalyst.

2. The reaction of benzene with polyvinyl alcohol in the presence of $AlCl_3$ was investigated. 1,3-Diphenylpentane was isolated from the liquid reaction products and characterized. It was established that in the presence of $AlCl_3$ the hydroxyl groups of polyvinyl alcohol are partially substituted by phenyl rings. The destructive phenomena increased on increasing the amount of catalyst and the duration of the reaction.

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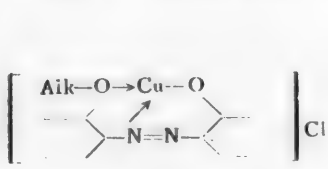
INTERNAL COMPLEX SALTS OF AZO COMPOUNDS

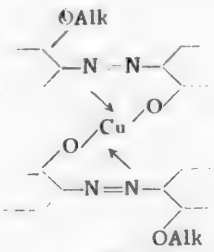
V. COPPERING OF o-HYDROXY-o'-ALKOXYAZO COMPOUNDS WITH SIMULTANEOUS DEALKYLATION

V. I. Mur

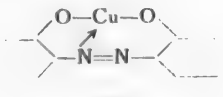
Previous reports [1] showed that depending on the conditions, o-hydroxy-o'-alkoxyazo compounds reacted with copper salts to give the following three types of complex.



(I)



(II)



(III)

Complex (I) formed under the mildest conditions and was converted to complex (II) when treated with bases, even at room temperature; the latter was also prepared by reacting the initial azo compound with copper salts in the presence of ammonia. On heating o-hydroxy-o'-alkoxyazo compounds with copper sulfate in the presence of such organic bases as pyridine or ethanolamine, coppering occurred simultaneously with dealkylation, which gave complex (III); the same complex was prepared by reacting complex (I) with the given organic bases.

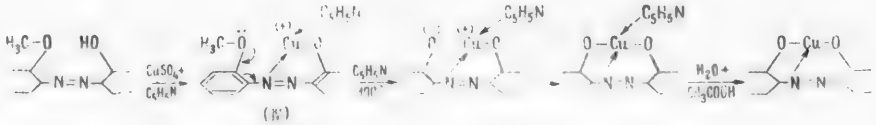
In the present work coppering of o-hydroxy-o'-methoxyazo compounds with simultaneous dealkylation was studied more closely to elucidate the role of complex formation in the dealkylation of these compounds and to determine if complexes (I) and (II) were intermediate compounds in this process. It also seemed interesting to trace the effect of substituents in the molecules of the o-hydroxy-o'-methoxyazo compounds on the capacity of the latter for dealkylation.

The study of this problem is not only of theoretical but also of practical value as the reaction studied is widely used for preparing direct azo dyes that are light-fast. However, in spite of the great number of patents [2], protecting copper complexes of o,o'-hydroxyazo dyes, and the methods of preparing them from the corresponding o-hydroxy-o'-methoxyazo dyes, we have not come across any information on the mechanism of coppering with simultaneous dealkylation. Although one paper [3] is devoted to the investigation of this reaction and a more thorough study was carried out on the effect of the conditions of treating o-hydroxy-o'-methoxyazo compounds with silver on their capacity for dealkylation, the nature of this reaction was not considered. The author's conclusions in this paper that the nitro group has no effect on dealkylation and that the sulfonic acid group hinders it cannot be considered sufficiently objective as comparisons were carried out under conditions that differed by more than one factor.

To elucidate the problems posed above, some o-hydroxy-o'-methoxyazo compounds and their copper complexes (I)and (II) were reacted with pyridine both in the presence and in the absence of copper salts and the degree of their dealkylation was determined. It was found that the starting azo compounds were not dealkylated, even when heated for a long time (40 hrs) at 100° with pyridine or a mixture of pyridine, ethyl alcohol and water. Their

copper complexes (I) and (II) were dealkylated under even milder conditions. The methyl group of the azo compound was eliminated when the reaction was carried out in the presence of copper salts. It was observed that the dealkylation, occurring when o-hydroxy-o'-methoxyazo compounds were reacted with equivalent and somewhat greater amounts of copper sulfate and pyridine, proceeded practically at the same rate as in the case of the corresponding complexes (I) with the same amount of pyridine, under the given experimental conditions. In the presence of a smaller amount of copper sulfate the azo compounds were dealkylated much more slowly. Complex (II) dealkylates with greater difficulty under the same conditions; although the addition of copper salts did accelerate the process, its rate did not attain the value of the dealkylation of complex (I). A rise in temperature and an increase in the amount of pyridine promoted dealkylation. Depending on their nature, the substituents in o-hydroxy-o'-methoxyazo compounds either facilitated or hindered dealkylation; according to their effect on the capacity of an azo compound for dealkylation (under the given experimental conditions), the substituents in the position para to the methoxyl group may be arranged in the following order: $NO_2 > H > OCH_3 > CH_3 > Cl$. A nitro group, located in the position meta to the methoxyl, hindered dealkylation. In all cases the color of the solution deepened before dealkylation.

The data obtained, together with the results of the previous investigation [1] on the reactions of the complexes, indicate that in the presence of pyridine or ethanolamine coppering of o-hydroxy-o'-methoyazo compounds with simultaneous dealkylation proceeded analogously to the dealkylation of complex (I), according to the following scheme:



Apparently complexes (I) and (II) are not intermediate stages in this reaction.

The formation of complex ion (IV) apparently explains the capacity of o-hydroxy-o'-methoxyazo compounds for dealkylation in the presence of copper salts and pyridine or other similar organic bases. Due to the copper atom attracting electrons from the nitrogen atom of the azo group, there is a displacement of electrons in this direction from the oxygen of the alkoxyl group and, as a result, the electron density of the oxygen decreases and the bond with the alkyl is weakened.

The data on the effect of substituents on the dealkylation capacity of azo compounds agree with the scheme proposed for this process. The nitro group in the position para to the alkoxyl, as an electronegative substituent affecting the chain of conjugated double bonds, attracted electrons from the oxygen atom and this weakened its bond with the alkyl and facilitated dealkylation. In the case of electron donor substituents, the reverse should happen and this actually occurred: methyl and methoxyl groups, in the position para to the alkoxyl, made dealkylation more difficult. A similar effect of a nitro group, in the position meta to the alkoxyl, and consequently in the position para to the azo group, was probably due to its attracting the electrons from the nitrogen atom of the azo group that was coordinated with the copper atom and this weakened the complex formation effect which affected the stability of the oxygen–alkyl bond.

EXPERIMENTAL

For the investigation we used anisole-(2-azo-1)-naphthol-(2) (V), (4-nitroanisole)-(2-azo-1)-naphthol-(2) (VI), (5-nitroanisole)-(2-azo-1)-naphthol-(2) (VII), (4-methoxyanisole)-(2-azo-1)-naphthol-(2) (VIII), (4-methylanisole)-(2-azo-1)-naphthol-(2) (IX) and (4-chloroanisole)-(2-azo-1)-naphthol-(2) (X), which were prepared by the usual method. Copper complexes of them with the composition 1 : 1 and 1 : 2 were prepared under the conditions adopted previously [1]. The new compounds were identified by analysis data and those described in the literature, by their melting points.

Reaction of azo compounds with pyridine. A solution of 0.5 g of the azo compound in 20 ml of pyridine in some experiments and in 50 ml of ethyl alcohol, 12.5 ml of pyridine and 1 ml of water in others was heated on a boiling water bath for 40 hrs, then the reaction mixture poured into 400 ml of water and the precipite which formed filtered off, washed with water and dried at 80°. The melting points of the substances obtained and the starting azo compounds were close; mixed samples of them melted practically without depression.

Reaction of copper complexes (I) and (II) of azo compound (V) with pyridine. A solution of 0.5 g of complex in 15 ml of pyridine in some experiments (a) and in 50 ml of ethyl alcohol, 5 ml of pyridine and 1 ml of water in others (b) was heated under reflux on a boiling water bath for 1 hr, then the reaction mixture quantitatively transferred into 400 ml of cold water and neutralized with acetic acid (to litmus) and the coagulated precipitate filtered into a tared Schott No. 2 funnel, washed with water until the smell of pyridine disappeared and dried to constant weight at 80°. The methoxyl group content of the substance obtained was determined by the Zeisel method and the percent of demethylation calculated.

Expt. no.	Designation of substance tested	Used in reaction (mole)		% demethylation found
		pyridine	$CuSO_4$	
1	(V)	0.028	0.002	16
2	(V)	0.028	0.0024	16
3	(V)	0.08	0.002	30
4	(V)	0.08	0.001	12
5*	(V)	0.2	0.002	83
6**	(V)	0.028	0.002	28
7	Complex (I) from (V)	0.08	0.002	32
8	Complex (II) from (V)	0.08	—	6
9	The same	0.08	0.001	13
10	(VI)	0.028	0.002	25
11	(VI)	0.08	0.002	55
12	Complex (I) from (VI)	0.08	—	54
13	Complex (II) from (VI)	0.08	—	12
14	(VII)	0.028	0.002	9
15	(VIII)	0.028	0.002	14
16	(IX)	0.028	0.002	7
17	(IX)	0.08	0.002	13
18	(IX)	0.14	0.002	19
19	Complex (I) from (IX)	0.028	—	6
20	Complex (II) from (IX)	0.028	—	1
21	(X)	0.028	0.002	6

* In Expt. 5, the reaction was performed without alcohol.

** In Expt. 6, cellosolve was used instead of alcohol.

The methoxyl group content in grams, found in the total amount of substance isolated (a), divided by the amount of starting material in grams (b) and multiplied by 100, corresponds to the percent methoxyl group content after demethylation. The ratio of the difference between the percent methoxyl group content of the starting material (c) and that obtained after dealkylation to the percent methoxyl group content of the starting material expresses the degree of demethylation. The value of the latter, multiplied by 100, corresponds to the percent of demethylation (x). After rearranging the equation obtained as a result of the above reasoning, the percent of demethylation may be calculated by the formula

$$x = 100\left(1 - \frac{100a}{b \cdot c}\right).$$

When the reaction was carried out under the conditions of experiment "a", complexes (I) and (II) of dye (V) were demethylated 80 and 45%, respectively, and under the conditions of experiment "b", 38 and 8%.

Reaction of azo compounds and their copper complexes (I) and (II) with copper sulfate and pyridine. To a hot solution of 0.002 mole of the azo compound or complex (I) or 0.001 mole of complex (II) in a definite amount of pyridine and 60 ml of ethyl alcohol was added a solution of the appropriate amount of copper sulfate in 1 ml of water and the reaction was performed and the substances obtained isolated and analyzed under the conditions of the previous experiment. The data from the experiments, carried out under these conditions with different compounds and amounts of reagents, are given in the table; in each case, the value of the percent of demethylations is the average result from two or three determinations.

SUMMARY

1. It was shown that dealkylation proceeded just as readily in reacting o-hydroxy-o'-methoxyazo compounds with an equivalent amount of copper sulfate and pyridine as in the corresponding complexes with a 1:1 composition, with the same amount of pyridine, all other conditions being equal; complexes with a 1:2 composition were more difficult to dealkylate.

2. It was found that, according to their effect on the dealkylation capacity of an azo compound reacted with copper sulfate and pyridine, substituents in the position para to the methoxyl group of o-hydroxy-o'-methoxyazo compounds may be arranged in the order: $NO_2 > H > OCH_3 > CH_3 > Cl$; a nitro group in a position meta to the methoxyl hinders dealkylation.

3. A scheme was put forward for the coppering of o-hydroxy-o'-alkoxyazo compounds with simultaneous dealkylation, which occurred when these compounds were reacted with copper salts and pyridine or other similar organic bases.

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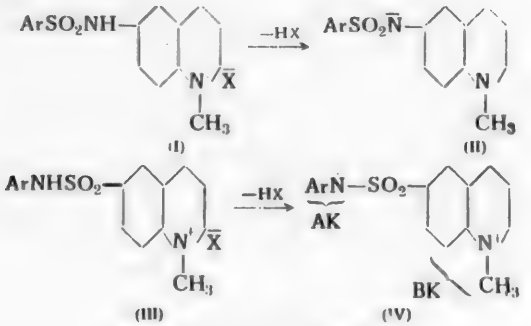
DIPOLAR IONS, FORMED BY THE ELIMINATION OF A PROTON FROM AN NH GROUP

XII. DERIVATIVES OF 6-QUINOLINESULFONIC ACID

A. M. Simonov

A study of quinoline salts, in particular the phenomenon of color in a series of these compounds, is of considerable interest as some representatives of this class are starting materials for the synthesis of dyes. In this work we studied the properties of quinolinium salts with a substituted sulfonamide group in the quinoline nucleus and the dipolar ions formed from them.

It was shown in previous reports [1] that quinolinium salts, containing an arylsulfamino group, may be converted to dipolar ions (betaines) by abstracting a proton from the NH group. Thus, for example, when treated with an aqueous ammonia solution, the methyl-p-toluenesulfonate of 6-p-toluenesulfamoquinoline (Ia) was converted into an orange dihydrate of 6-p-toluenesulfamoquinoline methylbetaine, which readily lost 2 molecules of water to form the anhydrous dipolar ion (IIa), which was bright red. The ease with which the quinolinium salt (Ia) was converted to a betaine was due to the NH group being affected by two systems possessing strong electron acceptor properties (the arylsulfonyl radical and the N-alkylquinolinium group).



For (I–IV): a. Ar = p-$CH_3C_6H_4$

b. Ar = p-$NO_2C_6H_4$

X = p-$CH_3C_6H_4SO_3$

As this work shows, the methylbetaine (IIb), containing a p-nitrobenzenesulfonyl radical, was formed even more readily from the quaternary salt than (IIa), under the action of pyridine; the higher lability of the hydrogen in the NH group, apparently, should be explained by an increase in the electron acceptor properties of the arylsulfonyl radical due to the introduction of a nitro group into it.

In order to study the effect of the onium N-atom on the lability of the NH group hydrogen, it seemed interesting to compare the properties of quinolinium salts I (a, b) with those of compounds isomeric to them, III (a, b), formed by melting methyl p-toluenesulfonate with anilides of 6-quinolinesulfonic acid. The quinoline nucleus in salts of structure (III) is connected to the NH group through an SO_2 group and as a result the onium N atom may affect the increase in lability of the NH hydrogen only by strengthening the electron acceptor properties of the acyl group.

One would expect that salt (IIIb) should, nevertheless, be readily converted into dipolar ion (IVb) as the NH group is affected by highly electrophilic groups – the p-nitrophenyl group and the acyl of the 6-quinolinesulfonic acid, whose electron acceptor properties are strengthened by the conversion of the N atom to the onium state. According to this hypothesis, betaine (IVb) is formed from the starting salt under the same conditions (treatment with bases that were equally weak) as the isomeric betaine (IIb).

On the contrary, the observation that the quinolinium salt (IIIa) was converted into a dipolar ion almost as readily as salt (Ia) was very unexpected. Although the NH group in this compound, in contrast to salt (Ia), was connected to only one strongly electrophilic radical, the effect of this radical on the NH group was so considerable that treatment of the onium salt even with a weak base (ammonia) resulted in the elimination of a proton and the formation of a dipolar ion (IVa).

Thus, isomeric salts with structures (I) and (III) reacted in the same way in weakly alkaline media. However, the reaction proceeded differently with caustic alkalis. In this case salt (I) was converted to a dipolar ion. However, if a hot aqueous solution of a salt with structure (III) was treated with excess caustic alkali, a betaine was not formed: the solution which was at first bright orange, gradually lost color and, after the excess alkali had been neutralized with acetic or dilute hydrochloric acid, it formed a precipitate that did not dissolve in excess acid and was slightly colored by impurities. Apparently this substance was a derivative of 1-methylquinoline. One could assume that the onium salt (III) was converted into a pseudo-base in a strongly alkaline medium; this conversion would be facilitated by the action of the $ArSO_2NH$ group, which would strengthen the effect of the onium N atom on the pyridine nucleus (cf. [2]). The pseudo-base remained in solution (due to the presence of the sulfamide group) and was oxidized by atmospheric oxygen to quinolone. We had observed the formation of a pseudo-base instead of a dipolar ion previously when some benzimidazolium salts, containing an arylamino group, were treated with alkaline agents [3].

The properties of the isomeric dipolar ions with structures (II) and (IV) did not depend noticeably on the order of connection of the $-SO_2N-$ group to the benzene and quinoline nuclei: the betaines (IV), like compounds (II) which are isomeric to them, dissolve in dilute acetic acid, are not hydrated when kept in water vapor and are brightly colored (dipolar ions (IIa) and (IVa) are bright red, (IIb) and (IVb) are bright yellow). According to the hypotheses put forward earlier, the strong deepening of the color in going from an onium salt to a dipolar ion is due to the formation in the molecule of a strongly electron donating chromophore,* an azeniate N atom (bonded dicovalently and with a negative charge) which has an effect when the molecule contains an electrophilic chromophore group (methinimonium, nitro group, quinoid nucleus, etc.) [5]. It should be noted that betaines (IVa) and (IVb) have almost the same deep color as compounds (IIa) and (IIb) although here the azeniate N atom is not conjugated with the electrophilic chromophore system (the methylquinolinium group). The deep color of these compounds may be explained on the basis of the investigations carried out by Izmail'skii and Solodkov on the color of molecular complexes of quinolinium salts with aromatic amines and amines of the quinoline series [6]. All these complexes have a deep color, which according to the authors is due to intermolecular reaction of the chromophore systems. Apparently, the color of betaines (IV) should also be explained by intermolecular reaction of separate electrophilic (BK) and electron donor (AK) components, included in the molecules of these compounds. It is nevertheless possible to conclude from a comparison of the color of betaines with structures (II) and (IV) that in considering the color phenomena in the series of dipolar ions containing conjugated chromophore systems, the possibility of intermolecular reaction in these systems, especially in crystalline compounds, should also be taken into account.

EXPERIMENTAL

6-p-Nitrobenzenesulfamoquinoline. This compound was prepared by the reaction of 6-aminoquinoline with p-nitrobenzenesulfonyl chloride in pyridine solution. The almost colorless, rectangular plates (from alcohol) had m. p. 227°.

Found %: S 9.68. $C_{15}H_{11}O_4N_3S$. Calculated %: S 9.74.

* See [4] for V. A. Izmail'skii's classification of chromophore systems.

Methyl p-toluenesulfonate of 6-p-nitrobenzenesulfamoquinoline (Ib). The yellowish white crystals (from dilute alcohol) had m. p. 264-265° (with decomp.). The salt was converted into a betaine by adding to it an aqueous solution of ammonia, pyridine or excess sodium acetate.

Found %: S 12.34. $C_{23}H_{21}O_7N_3S_2$. Calculated %: S 12.44.

Methylbetaine of 6-p-nitrobenzenesulfamoquinoline (IIb). The compound was prepared by adding a small excess of ammonia to a hot (80°) aqueous solution of the quaternary salt. The dark yellow precipitate was washed with water and dried in a desiccator over sodium hydroxide. The betaine was insoluble in dioxane, acetone and chloroform, difficultly soluble in alcohol and in hot nitrobenzene and pyridine but readily soluble in a mixture of pyridine and water, from which it crystallized as bright yellow needles; it also dissolved in dilute acetic acid. It was not hydrated in water vapor. The decomposition point of the betaine was at about 280°.

Found %: S 9.31, 9.35. $C_{16}H_{13}O_4N_3S$. Calculated %: S 9.34.

6-Quinolinesulfonyl chloride. 4 g of 6-quinolinesulfonic acid, dried at 110-120°, was heated with an equimolecular amount of phosphorus pentachloride (4 g) for 2 hrs at 110-120°. The mixture was cooled and then treated simultaneously with ice and an ice-cooled 10% solution of soda. The filtrate was sucked off and the acid chloride dissolved in benzene. The benzene solution was washed with soda solution and dried with calcium chloride. The benzene was distilled off and the residue recrystallized from low-boiling benzine. The snow-white crystals had m. p. 88.5-89°. The compound rapidly decomposed with hot water to form a clear solution.

Found %: Cl 15.36; S 13.95. $C_9H_6O_2NSCl$. Calculated %: Cl 15.57; S 14.05.

p-Toluidide of 6-quinolinesulfonic acid (6-N-p-tolylsulfamidoquinoline). The 6-quinolinesulfonyl chloride was added to a solution of an equimolecular amount of p-toluidine in dry pyridine. The following day, the solution was poured into water. The precipitate was carefully washed with hot water and recrystallized twice from dilute alcohol. The colorless crystals were soluble in dilute sodium hydroxide solution. The m. p. was 189.5-190°.

Found %: S 10.67. $C_{16}H_{14}O_2N_2S$. Calculated %: S 10.75.

Methyl p-toluenesulfonate of 6-[N-(p-tolyl)-sulfamido]-quinoline (IIIa). The yellowish white crystals (from a mixture of alcohol and ether) had m. p. 220-222° (with decomp.).

Found %: S 12.99. $C_{24}H_{24}O_5N_2S_2$. Calculated %: S 13.23.

When a concentrated aqueous solution of the salt was treated with a small excess of ammonia, the solution became red-orange and a precipitate of orange needles of the betaine was formed on standing. The addition of alkali to a hot aqueous solution of the salt gave a red-orange solution, whose color rapidly paled. If this solution, which had a pale pink color due to traces of side products, was neutralized with acetic acid or treated with an excess of ammonium chloride, a pale pink precipitate was formed, which was readily soluble in alkalis, acetone and pyridine and almost insoluble in dilute acids. This product, which was not examined more closely, was apparently a 1-methylquinoline derivative.

Methylbetaine of 6-[N-(p-tolyl)-sulfamido]-quinoline (IVa). Ammonia was added dropwise to a hot solution of 0.48 g of the quaternary salt in 8 ml of water until there was a faint smell. The red-orange precipitate formed was sucked off, carefully washed with water and dried in a desiccator over alkali. The bright red lustrous crystals (needles) became orange in color when ground up. The yield was 0.23 g. The betaine was soluble in dilute acetic acid and insoluble in pyridine. The product was recrystallized from 90% acetic acid; it melted at about 235° (with decomp.). The betaine was not hydrated on standing in water vapor.

Found %: S 10.26, 10.15. $C_{17}H_{16}O_2N_2S$. Calculated %: S 10.26.

p-Nitroanilide of 6-quinolinesulfonic acid. The compound was prepared by reacting p-nitroaniline with 6-quinolinesulfonyl chloride in pyridine. The colorless crystals (from alcohol) with m. p. 242-243°, were soluble in dilute alkali and an aqueous solution of ammonia to give a yellow color.

Found %: S 9.70. $C_{15}H_{11}O_4N_3S$. Calculated %: S 9.74.

Methyl p-toluenesulfonate of 6-[N-(p-nitrophenyl)-sulfamido]-quinoline (IIIb). The pale yellow crystals (from dilute alkali) had m. p. 266-267°.

Found %: S 12.32. $C_{23}H_{21}O_7N_3S_2$. Calculated %: S 12.44.

When the salt was treated with ammonia (slight excess), soda or pyridine, it was converted into the betaine. Treatment of a solution of the quaternary salt with sodium hydroxide did not give a dipolar ion: the originally orange solution became yellow and, on acidification, deposited a pale colored precipitate, which was almost insoluble in excess acid.

Methylbetaine of 6-[N-(p-nitrophenyl)-sulfamido]-quinoline (IV b). A hot solution of 0.52 g of the quaternary salt in 12 ml of 40% alcohol was treated with a slight excess of ammonia. Cooling the solution yielded a yellow precipitate (0.32 g), which was recrystallized from dilute alcohol and dried in a desiccator over phosphorus pentoxide. The fine yellow needles were soluble in dilute acids and in hot nitrobenzene and difficultly soluble in acetone and pyridine. The melting point, depending on the rate of heating, lay between 237 and 245°. The compound was not hydrated on standing in water vapor.

Found %: S 9.33, 9.29. $C_{16}H_{13}O_4N_3S$. Calculated %: S 9.34.

SUMMARY

1. Quinolinium salts, of structure (III a, b), which are 6-quinolinesulfonic acid derivatives, were synthesized. It was shown that treatment of these salts with weakly alkaline agents eliminated a proton from the NH group and gave dipolar ions as in the case of isomeric salts (I).

2. It was established that quinolinium salts (III), in contrast to (I), were not converted to betaines by treatment with excess caustic alkali.

3. The reasons for the color of dipolar ions with structure (IV) were discussed.

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** In Russian.

CONDENSATION OF 6-QUINOLINEALDEHYDE WITH KETONES AND ESTERS

B. P. Lugovkin

In developing our previous work on the study of the chemical properties of 6-quinolinealdehyde [1] we investigated its condensation with ketones and some esters.

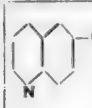
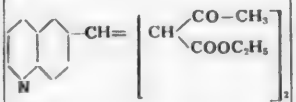
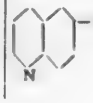
By reacting the aldehyde with acetone in a dilute aqueous alkaline solution we were able to obtain quinolidene-(6)-acetone (I) in 33% yield. A high polymer product was prepared in an alcohol solution in the presence of sodium ethoxide.

The aldehyde reacted readily with acetophenone in the presence of sodium ethoxide. This gave a 71% yield of quinolidene-(6)-acetophenone (II).

The aldehyde was reacted with acetoacetic ester in the presence of pyridine with cooling of the reaction mixture [2]. Only the diethyl ester of quinolene-(6)-bis-acetoacetic acid (III) could be isolated from the reaction products in a 33% yield. The aldehyde condensed with ethyl acetate to give ethyl quinolyl-(6)-acrylate (IV) in 22% yield.

The condensation product of the aldehyde with diethyl malonate was identified as the methiodide of diethyl quinolidene-(6)-malonate (V). The ester yield was 49%.

Condensation of the aldehyde (2 moles) with diethyl succinate in the presence of sodium ethoxide and piperidine did not give diethyl α,δ-diquinolyl-(6,6')-fulgenate [2].

Expt. no.	Formula	Condensation product			Methiodide		
		melting point	N (in %)		melting point	Iodine (in %)	
			found	calc.		found	calculated
I		112—112.5°	6.83	7.10	236—237°	37.62	37.43
II		146—146.5	5.74	5.40	245—247	31.59	31.64
III		151—152	3.98	3.50	195—196	23.30	23.45
IV		Thick liquid	5.82	6.16	202—204	34.02	34.39
V		Thick liquid	—	—	182—184	28.40	28.77

EXPERIMENTAL

All the experiments required anhydrous 6-quinolinealdehyde (m. p. 75-76°).

Condensation with acetone.* 3 ml of 2 N sodium hydroxide solution was added to 4 g of the aldehyde and 8 g of acetone in 200 ml of water. The mixture was kept for 48 hrs (with periodic shaking) and then the thick liquid produced was extracted with chloroform. Drying with sodium sulfate and removal of the solvent yielded 4.2 g of a solid residue. Extraction of the mixture with benzine (13 ml) and benzene (2 ml) gave 1.66 g of crystals with m. p. 111-112° (a tarry product was left in the sleeve). A second recrystallization produced light yellow crystals. The substance was readily soluble in organic solvents, difficultly soluble in light benzine and dissolved in warm water. The picrate had m. p. 180° (from glacial acetic acid).

The phenylhydrazone consisted of yellow crystals with m. p. 169° (recrystallized from benzene).

Found %: N 14.68. $C_{19}H_{17}N_3$. Calculated %: N 14.63.

Methiodide. When 0.3 g of the substance and 0.6 ml of methyl idodide were kept for 3 days, they yielded 0.37 g of dark yellow crystals (after washing with hot anhydrous alcohol). The substance dissolved when heated in water, with great difficulty in alcohol and was insoluble in ether.

Condensation with acetophenone. A solution of sodium ethoxide (0.5 g of metallic sodium in 10 ml of alcohol) was added to 5 g of aldehyde and 4.3 g of acetophenone in 5 ml of anhydrous alcohol; the temperature rose to 27° and a crystalline product rapidly separated. After dilution, washing with water and recrystallization from alcohol, the product yielded 5.86 g of crystals with m. p. 145-146°. The substance was recrystallized from benzene. It dissolved readily in alcohol and benzene on heating, with difficulty in ether and was insoluble in water. The picrate had m. p. 233° (from glacial acetic acid).

The phenylhydrazone formed light yellow crystals with m. p. 178° (recrystallized from dioxane).

Found %: N 11.89. $C_{24}H_{19}N_3$. Calculated %: N 12.03.

Methiodide. From 0.5 g of the substance and 1 ml of methyl iodide (under the conditions of the previous experiment) we obtained 0.6 g of yellow crystals (after washing with hot, anhydrous alcohol). The product dissolved in water on heating, with great difficulty in alcohol and was insoluble in ether.

Condensation with acetoacetic ester. A solution (−5°) of 0.5 g of piperidine in 2 ml of anhydrous alcohol was added to 5 g of aldehyde ** and 4.3 g of ester at −5°. The mixture was kept in the cold (on the average 0-5°) for 48 hrs and washed with cold and then hot water to give a thick liquid, which crystallized on standing. Recrystallization from benzene (5 ml) with cooling, yielded 2.2 g of crystals with m. p. 146°, which formed white microcrystals after a second recrystallization. The substance dissolved in alcohol, benzene and dioxane on heating. The picrate had m. p. 185-186° (from glacial acetic acid).

Methiodide. By heating 0.3 g of the substance with 0.5 ml of methyl iodide on a water bath for 0.5 hours, we obtained 0.25 g of light yellow crystals (recrystallized from anhydrous alcohol). They dissolved in water with heating, in alcohol with difficulty and were insoluble in ether.

Condensation with ethyl acetate. To a solution of ethyl sodioacetate, prepared from 0.95 g of metallic sodium in 20 g of ester, cooled in snow, was added a cooled solution of 6.4 g of aldehyde in 9 g of ester. The mixture was kept at room temperature for 1 hr and then 5 ml of glacial acetic acid was added followed by water until the ester layer had separated completely. After removal of the solvent, the residue was vacuum distilled. A fraction with b. p. 153-186° (1 mm) isolated was redistilled; we obtained 2 g of a very thick liquid with b. p. 198-201° (6-7 mm), $n^{20}D$ 1.6369, d^{20}_{20} 1.0641. The picrate had m. p. 238-239° (from glacial acetic acid).

Methiodide. By heating 0.25 g of the substance with 0.5 ml of methyl iodide on a water bath for 0.5 hrs, we obtained 0.35 g of golden yellow crystals (recrystallized from anhydrous alcohol). They dissolved in water, in alcohol on heating and were insoluble in ether.

* Condensations under other conditions did not lead to the desired results; in every case, tarry products were obtained.

** Compound (III) required 2.59 g of aldehyde.

Condensation with diethyl malonate. 0.5 g of piperidine was added to 4 g of aldehyde and 4.08 g of ester; the temperature rose to 16°. After standing for 48 hrs, the mixture was heated on a water bath for 2 hrs. The product was washed with hot water and dried in ether solution with sodium sulfate to yield 7.4 g of an oily liquid, which did not distill in vacuum (4 mm). The picrate had m. p. 196-198° (from glacial acetic acid).

Methiodide. By keeping 1.08 g of the substance and 1.5 ml of methyl iodide for 3 days, we obtained 0.8 g (which corresponds to 3.71 g of ester) of dark yellow crystals (recrystallized from anhydrous alcohol with active charcoal). They dissolved in water and alcohol with heating and were insoluble in ether.

SUMMARY

6-Quinolinealdehyde was condensed with acetone, acetophenone, acetoacetic ester, ethyl acetate and diethyl malonate. The condensation products were characterized as methiodides.

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*** In Russian.

REACTION OF DIAZO COMPOUNDS WITH SULFAMIC ACID AND ITS DERIVATIVES

IX. REASONS FOR THE COLOR OF DIAZONIUM SALTS OF ARYLSULFAMIC ACIDS

D. Z. Zavel'skii and L. A. Lishnevskaia

In a previous report [1] it was shown that diazonium chlorides undergo salt exchange with the sodium salts of arylsulfamic acids, to form diazonium salts of arylsulfamic acids:

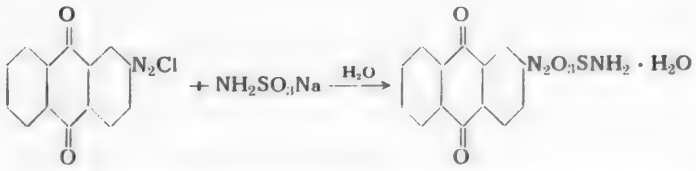
$$Ar—N_2Cl + NaO_3SNH—Ar' \longrightarrow Ar—N_2O_3SNH—Ar' + NaCl$$

When an electron acceptor substituent is present in the benzene nucleus of the diazo cation, these salts crystallize well from aqueous solutions and, in the solid form, are deeply colored from golden yellow and red to almost black. It was established that the more electronegative the substituents in the benzene nucleus of the diazo cation and the higher their capacity for electron attraction, the less water-soluble were the corresponding arylsulfamates and the deeper their color. The color also deepened on introducing electron donor substituents into the benzene nucleus of the arylsulfamic acid.

Diazonium arylsulfamates, deeply colored in the solid state, dissolved in water to form much lighter and weaker colored solutions. A study of the absorption spectra of aqueous solutions of various concentrations showed that they did not follow the Lambert-Beer law due to dissociation of the arylsulfamates into the colorless ions forming them.

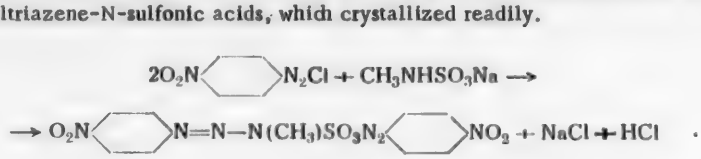
The properties of diazonium arylsulfamates which are quite unusual in comparison with most other diazonium salts, induced us to attack the problem of what there was exactly in the structure of arylsulfamic and, in particular, phenylsulfamic acids, which caused the deep color of their diazonium salts. First of all, it was interesting to determine whether the unsubstituted acid itself or its alkyl derivatives were capable of giving colored diazonium salts, i. e., did the phenyl nucleus of phenylsulfamic acid have a definite role.

A series of control experiments showed that diazo compounds of the benzene series reacted with unsubstituted sulfamic acid in an acid medium to give colorless solutions from which solid salts could not be isolated. Prolonged research established that 2-anthraquinonyldiazonium chloride, which itself was golden yellow, reacted with the sodium salt of sulfamic acid to give crystalline 2-anthraquinonyldiazonium sulfamate.



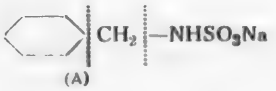
The structure of this salt, containing one molecule of water of crystallization was established by quantitative coupling with β-naphthol (giving the diazo component content), titration with nitrite (sulfamic acid content) and diazo nitrogen determination. It was found that 2-anthraquinonyldiazonium sulfamate had the same golden yellow color as the chloride. Consequently, the relatively weak color of the salt depends not on the nature of the anion but on the nature of the diazo cation, containing the anthraquinone ring. That means that unsubstituted sulfamic acid is incapable of giving salts of deep color with diazo compounds.

We previously studied [2] the reaction of methylsulfamic acid with diazo compounds in an acid medium. It was established that methylsulfamic acid did not form salts of the $ArN_2O_3SNHCH_3$ type under these conditions but underwent diazoamino condensation with nitrodiazobenzene and 2,5-dichlorodiazobenzene, to precipitate diazonium salts of methylaryltriazene-N-sulfonic acids, which crystallized readily.



These salts are colored from light yellow to yellow in the case of p-, m- and o-nitrodiazobenzene and in the case of 2,5-dichlorodiazobenzene, the salt first precipitates as colorless needles, which gradually changed into yellow cubes. Consequently, methylsulfamic acid, even substituted with a nitrophenylazo radical (containing a chromophore), is incapable of giving deeply colored salts with aryldiazo cations.

One may conclude from this that the formation of deeply colored diazo salts occurs only when the sulfamic group is connected directly to the conjugated system of the benzene nucleus. To confirm this conclusion we synthesized the sodium salt of benzylsulfamic acid in which the benzene ring is separated from the sulfamic group by a methylene bridge (A).



(A)

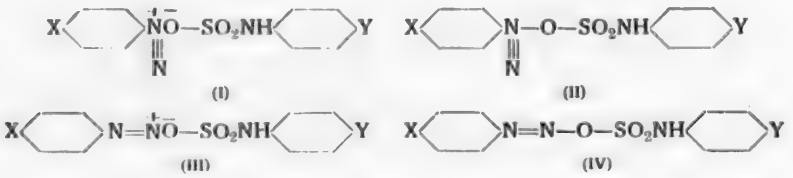
It was found that in a mineral acid medium, benzylsulfamic acid was incapable of precipitating salts with diazo compounds and instead the free acid itself separated from the solution. Such behavior may be explained by the fact that benzylsulfamic acid is a much weaker acid than phenylsulfamic acid, as the ionization constant at 25° is equal to $3.0 \cdot 10^{-10}$ for aniline and $2.4 \cdot 10^{-5}$ for benzylamine. When the salt exchange was carried out in an acetic acid medium instead of a mineral acid one, crystalline 4- and 3-nitrophenyldiazonium benzylsulfamates could be isolated and both were light yellow in color.

Acetic acid solutions of 4-chloro-, 2-nitro- and 4-nitro-2-methylphenyldiazonium did not form solid benzylsulfamates, apparently due to their ready solubility and the reaction solutions were colorless. Under those conditions, 2,5-dichloro- and 4-nitro-2-chlorodiazobenzene also formed light yellow, but unstable diazo salts which were rapidly converted into diazoamino compounds and tar.

It was established that the separation of the sulfamic group from the benzene ring using, for example, a methylene bridge, as occurs in benzylsulfamic acid, breaks down the mechanism which brings about the deep color of the diazonium salts of arylsulfamic acids. In other words, the bathochromic effect in such salts is observed only when the conjugated system of the benzene nucleus is connected directly to the sulfamic group which forms a salt link with the diazo compound, and this, in its turn, represents a system of a benzene ring, connected to a diazo group.

It has already been noted that by increasing the electronegativity of the substituent in the benzene nucleus of an arylsulfamic acid, one can obtain gradually deeper and deeper colored salts. It is logical to assume from this that the conjugation effect between the electron acceptor cation and electron donor anion, without which color is impossible, is transmitted through the salt link. However, as conjugation in colored organic bodies is realized only through covalent bonds, it would be useful to examine in greater detail the character of the bond between the cation and the anion in the compounds, which we have called diazonium arylsulfamates.

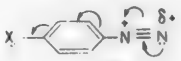
The structure of arylsulfamates of diazo compounds may be represented by Formulas (I)-(IV).



(I) (II)

(III) (IV)

In Formula (I) the bond between the ions may, at first glance, be considered as purely electrovalent, characteristic of quaternary nitrogen salts. However, due to the free electron pair of the terminal nitrogen, there is conjugation in the diazonium cation which results in the formation of a fractional positive charge on the terminal nitrogen atom and in a corresponding decrease in the positive charge of the second nitrogen (B).



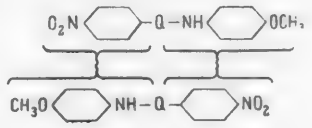
(B)

The more electronegative the substituent X, the lower the electron density at the terminal nitrogen and the greater the similarity of the structure of the salt to Formula (III). However, the salts of strong mineral acids with diazo compounds have a structure which is much more accurately described by Formula (I). I. V. Grachev [3], who arrived at the same conclusion by studying the properties of diazo compounds by potentiometric titration of their aqueous solutions with a glass electrode, found that the pH value of 4-nitrophenyldiazonium chloride equals 5.6. The pH values we measured for 4-nitrophenyldiazonium phenyl- and 4-tolylsulfamates [1] were found to be the same and equal to 5.7. The closeness of the pH values of chlorides and arylsulfamates of diazo compounds indicates that the latter, too, should be assigned the diazonium formula (I). This formula is also supported by the fact that the arylsulfamates of diazo compounds are formed as a result of exchange between diazonium chlorides and sodium arylsulfamates in a mineral acid medium and that they are readily soluble in water and dissociate into the original colorless ions. Formula (II) should be rejected as it contains pentacovalent nitrogen, and Formula (IV) is unsuitable as it assumes a covalent bond between the ions.

As is known, the modern theory on color of organic compounds holds that color, i. e., the displacement of light absorption towards the long wavelength part of the spectrum, is due to the presence in the organic compound of a system of conjugated double bonds which has at its ends electron donor and electron acceptor groups held together by a conjugated system with a tendency to form dipoles [4]. In the case of diazonium arylsulfamates, however, formed similarly to type (I), substituents X and Y are conjugated by a system which is interrupted by the salt link.

As is known, V. A. Izmail'skii and co-workers showed, as a result of extensive and thorough work [5], that with two conjugated systems with sufficiently strong electron acceptor and electron donor substituents at the ends, color may be observed even in substances in which the two systems are separated from each other by some group Q, incapable of conjugation. For example, while nitrobenzene and aniline are colorless, 4-nitrobenzylanilide [6] is yellor or orange in color (there are two forms) and 4-nitro-4'-methoxybenzylanilide is red [7].

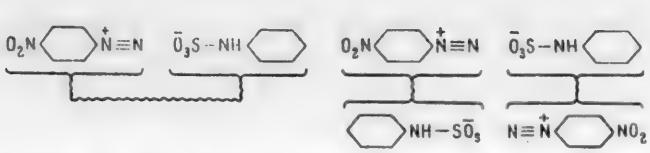
Izmail'skii considered that the reason for color in such bodies is an intermolecular reaction of the electron donor and the electron acceptor systems, which he represented in the following schematic form:



This type of reaction is known to occur between nitro compounds or quinones and arylamines, phenols, etc., and is being investigated carefully by a number of authors. In particular, Izmail'skii and other studied the reaction of nitrobenzene with dimethylaniline. They found that while nitrobenzene in a pyridine solution has λ_{max} 309 mμ and dimethylaniline 315 mμ, then p-nitro-N-dimethylaniline has λ_{max} 395 mμ and a solution of dimethylaniline in excess nitrobenzene – 430 mμ.

On this basis, Izmail'skii considered that in certain cases intermolecular reaction may play a very important part as a color factor in dyes.

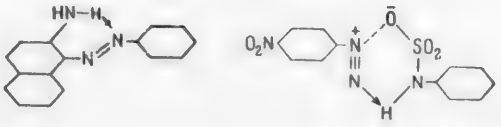
From the reasons given above one may suppose that the reaction of the arylsulfamate anion with a diazo cation in solution and in the crystalline form is also intermolecular according to the following scheme:



In this case salt formation only brings the electron donor and electron acceptor systems into sufficiently close proximity.

However, special experiments showed that on dissolving sodium phenyl- or tolylsulfamates in alcohol and diluting these solutions with nitrobenzene or dinitrochlorobenzene (electron acceptor systems), like acetanilide or benzenesulfonylsulfanilic acid ($C_6H_5NHSO_2C_6H_4SO_3H$), no deepening of color was noticed. Consequently, the reason for color in diazonium arylsulfamates is actually salt formation and not intermolecular reaction.

It is known that in o-aminoazo dyes there is a hydrogen bond between the amino group hydrogen and one of the nitrogens in the azo group, due to the unshared electron pair on the latter. Such a hydrogen bond, causing a definite change in the electron structure of the arylazo radical and the formation of an additional ring, is the reason for the deepening of color, especially when the hydrogen is substituted by a metal. Considering that the terminal nitrogen in a diazonium cation also has an unshared electron pair, we considered that a hydrogen bond could also form in diazonium arylsulfamates, which for the same reason would also cause a deepening in the color:



o-Aminoazo dye 4-Nitrophenyldiazonium salt of phenylsulfamic acid

To determine whether this hypothesis was correct, we synthesized N-ethylphenylsulfamic acid, which has not been described in the literature, by sulfonating N-ethylaniline with anhydropyridinesulfonic acid in pyridine. This arylsulfamic acid, in which the amino group hydrogen was substituted by an ethyl group gave salts with 4-chloro-, 3-nitro- and 4-nitrophenyldiazoniums, colored brownish-yellow, orange-red and reddish brown, respectively. A comparison of these salts with those synthesized earlier from the corresponding phenylsulfamates showed that the ethyl derivatives were only slightly ligther in color. The rest of the properties of diazonium ethylphenylsulfamates were also found to be quite similar to those of phenylsulfamates, the only difference being that they were somewhat less stable to storage in a dry form and to even slight heating in water. 2,5-Dichloro- and 2-chloro-4-nitrophenyldiazonium salts of ethylphenylsulfamic acid could not be prepared, as instead of them, water-insoluble products of diazo salts rearranging to diazoamino compounds were formed. The same result was obtained on reacting these diazoniums with phenyl- and tolylsulfamic acids [1].

From these experiments one may conclude that the presence of hydrogen on the amino group of an arylsulfamic acid results only in a certain stabilization and slight deepening of the diazo salt colors and that the substitution of hydrogen by the ethyl group does not interfere with the conjugation of the electron donor and electron acceptor systems, connected by the salt bond. Consequently, the main reason for color in diazonium arylsulfamates is the presence of a salt bond of a special character between its component ions and which is capable of transmitting the conjugation effect between the latter.

EXPERIMENTAL

Synthesis of sodium benzylsulfamate. Benzylamine was synthesized by the method of Ing and Manske [8]. The barium salt of benzylsulfamic acid was synthesized using Paal and Lowitsch's procedure [9]. The sodium salt of benzylsulfamic acid, which is not described in the literature, was prepared by the following method. A concentrated aqueous solution of 9.7 g of Glauber's salt was added to 15.3 g of barium benzylsulfamate. The reaction mixture was heated to 55-60° and the precipitate of barium sulfate filtered off and washed with a small amount of hot water. Cooling the combined filtrate and wash water in ice yielded a crystalline precipitate of sodium benzylsulfamate, which was separated by filtration. The rest of the sodium salt was obtained by evaporating the mother liquors. The pure product was obtained by recrystallization from alcohol.

Benzylsulfamic acid and its salts may be determined by nitrosation with nitrite in an acid medium.

0.2365 g of substance: 11.2 ml 0.1 N nitrite solution. $C_7H_8O_3NSNa$. Calculated: 11.3 ml of 0.1 N sodium nitrite solution.

Synthesis of sodium N-ethylphenylsulfamate. Technical monoethylaniline was freed from aniline and diethylaniline by the method of Blume and Kloffler [10], which gave good results. The purified monoethylaniline was sulfonated by the method described in a French patent [11] for monomethylaniline. By changing the method, it was possible to obtain an end product of good quality in high yield. 225 ml of pyridine was placed in a three-necked flask, fitted with a stirrer, a thermometer and a dropping funnel and externally cooled in an ice–salt mixture, and 64 g of chlorosulfonic acid was added dropwise at −10° at such a rate that the temperature did not rise above 5°. After the addition, the temperature of the mixture was allowed to rise to 20°, 60.5 g of ethylaniline added and the mixture heated for 2 hrs at 60-70°.

The mixture was cooled to 20°, poured into a suspension of soda in water and the pyridine removed by steam distillation. The residue in the flask was cooled, when it deposited a voluminous precipitate of coarse, brownish crystals. The precipitate was filtered off, washed first with water and then with alcohol and ether and dried. The yield was 88%.

After 2 recrystallizations from alcohol, it formed coarse white crystals with a hardly noticeable brownish tinge and a strong silky sheen.

Found %: Na 10.2. $C_8H_{10}O_3NSNa$. Calculated %: Na 10.3.

Reactions of benzylsulfamic acid with diazonium chlorides in a mineral acid medium. An aqueous solution of sodium benzylsulfamate, saturated at room temperature, was cooled in an ice bath. With vigorous stirring, concentrated hydrochloric acid solutions of phenyl-, 4-chlorophenyl-, 2,5-dichlorophenyl-, 4-nitrophenyl- and 4-nitro-2-chlorophenyldiazonium chlorides were added to this solution. The diazonium chloride solutions were prepared by the method described in the previous report [1].

In all cases, the solutions first obtained deposited colorless or pale yellow crystals – plates, which were readily soluble in water and coupled with azo components more or less vigorously. Analysis showed that the precipitate was free benzylsulfamic acid, containing a little diazonium compound.

Consequently, in a hydrochloric acid medium, benzylsulfamic acid, liberated from its sodium salt, is incapable of displacing hydrochloric acid from its aryldiazonium salts.

Reaction of sodium benzylsulfamate with diazonium acetates. A saturated solution of sodium acetate was added to a hydrochloric acid solution of a diazo compound until the pH reached 3-4. The acetic acid diazo solution obtained was added with cooling and stirring to an aqueous suspension of sodium benzylsulfamate.

4-Nitrophenyldiazonium salt of benzylsulfamic acid. When 4-nitrophenyldiazonium was added to a suspension of sodium benzylsulfamate, a voluminous, pale yellow precipitate of coarse, lustrous crystals was immediately deposited. Under a microscope the crystals appeared as broad tablets with bevelled edges. The precipitate was recrystallized from water heated to 60°. The recrystallized precipitate was brighter yellow in color as the crystals were bigger. It was washed with ice water, pressed out first on the filter and then on porous plate and dried in vacuum over solid alkali, spread out as a very thin layer. The diazo salt dissolved completely in cold water and coupled vigorously with azo components. When heated in the dry state it decomposed with an explosion.

Found %: N 16.49; S 9.25; diazo nitrogen 8.53. $C_{13}H_{12}O_5N_4S$. Calculated %: N 16.66; S 9.53; diazo nitrogen 8.33.

3-Nitrophenyldiazonium benzylsulfamate. An acetic acid solution of 3-nitrophenyldiazonium was poured into a concentrated solution of sodium benzylsulfamate and after 2-3 min, a light yellow precipitate formed. Under a microscope it appeared as elongated plates. The precipitate was filtered off, washed with ice–water, pressed out on a porous plate and dried in vacuum. The substance was almost completely soluble in water, coupled vigorously with azo components and decomposed with an explosion when heated in the dry form.

Found %: diazo nitrogen 8.49. $C_{13}H_{12}O_5N_4S$. Calculated %: diazo nitrogen 8.33.

Sodium benzylsulfamate and acetic acid solutions of diazobenzene and 4-chloro-, 2-nitro- and 4-nitro-2-methyldiazobenzenes. When acetic acid solutions of the diazo compounds listed were poured into thick suspensions of sodium benzylsulfamate, the color of the solutions did not change and no precipitates were formed.

Sodium benzylsulfamate and 4-nitro-2-chlorodiazobenzene. When the diazo solution was poured into a suspension of sodium benzylsulfamate, a light yellow precipitate formed immediately. We were unable to isolate it as it rapidly changed into an orange tar, which gradually reddened. The change was complete in a few minutes. The tar was almost insoluble in water and gave a weak reaction for active diazo compound. Attempts to stop the reaction at the formation of the diazo sulfamate were unsuccessful.

Sodium benzylsulfamate and 2,5-dichlorodiazobenzene. An acetic acid solution of the diazo compound was combined with a suspension of the benzylsulfamate. A light yellow precipitate gradually separated and under a microscope it appeared as needles. The filtered and washed precipitate was insoluble in water, but dissolved readily in glacial acetic acid. The addition of α-naphthylamine to the acetic acid solution and gentle heating produced an intense color, characteristic of diazo compounds.

Reaction of sodium N-ethylphenylsulfamate with diazonium chlorides. 4-Nitrophenyldiazonium N-ethylphenylsulfamate. When the diazo solution was added to a suspension of ethylphenylsulfamate, the reaction mixture acquired a red-brown color. The precipitate, which rapidly appeared, gradually increased. It consisted of coarse, brick red crystals with a gold luster, which appeared as broad plates under a microscope. The substance had all the properties of a diazonium salt; it was completely soluble in water, coupled readily with azo components in a neutral medium and decomposed with an explosion, when heated in the dry state.

We were unable to purify the substance by recrystallization as in contact with water heated to 50°, it immediately formed a tar. The diazo salt obtained was very unstable on storage. After several hours, even in vacuum, it decomposed, forming a liquid, tarry mass. For analysis we had to use an unpurified sample of the diazo salt, freshly precipitated and dried in vacuum on a porous plate.

Analysis for diazo component content. To a solution of a sample of the substance in cold water was added excess 0.1 N β-naphthol solution, adjusted to pH 7 by the addition of acetic acid. The solution was kept for 20 min and the excess β-naphthol then titrated with a 0.1 N solution of p-nitrophenyldiazonium.

0.7284 g of substance: 19.70 ml of 0.1 N β-naphthol solution. $C_{14}H_{14}O_5N_4S$. Calculated: 20.74 ml of 0.1 N β-naphthol solution.

3-Nitrophenyldiazonium N-ethylphenylsulfamate. When the components were mixed, the mixture acquired a pale red color, which gradually became intense. Simultaneously, a lustrous orange-red precipitate formed. The filtered precipitate consisted of coarse orange-red plates, which were readily soluble in cold water and coupled with azo components readily.

The substance was so unstable that we were unable to recrystallize it from warm water.

Analysis for diazo component content: 0.6238 g of substance: 16.9 ml of 0.1 N β-naphthol solution. $C_{14}H_{14}O_5N_4S$. Calculated: 17.8 ml of 0.1 N β-naphthol solution.

4-Chlorophenyldiazonium N-ethylphenylsulfamate. The diazo solution was added to a suspension of ethylphenylsulfamate. The reaction solution gradually colored, changing from pale yellow-orange to red. A small lustrous precipitate appeared. After the addition of a saturated solution of sodium acetate and cooling of the reaction mixture, a thick paste of crystals was formed and under a microscope, these appeared as plates. The precipitate was filtered off, washed with ice–water and pressed out on a porous plate, spread out as a very thin layer. The dehydrated precipitate had a browish yellow color with a gold luster; it dissolved almost completely in water to form a slightly yellow solution and coupled vigorously in neutral solution with H-acid and R-salt. During attempted recrystallizations from warm water and also on storage, even for a few hours, the substance decomposed.

Analysis for diazo component content: 0.5986 g of substance: 16.9 ml of 0.1 N β-naphthol solution. $C_{14}H_{14}O_3N_3SCl$. Calculated: 17.6 ml of 0.1 N β-naphthol solution.

Sodium N-ethylphenylsulfamate and 4-nitro-2-chlorophenyldiazonium chloride. When the diazo solution was added to the suspension of ethylphenylsulfamate, the solution acquired an intense red-brown color. After several minutes, a fine, light brown precipitate formed. When filtered off and washed, the precipitate was insoluble

in water. Under a microscope, it appeared as very fine, yellow crystals. The substance did not couple with an azo component in an aqueous solution. Consequently, it was not a diazo salt. It gave an intense color with α-naphthylamine in glacial acetic acid, which is characteristic of diazoamino compounds.

Sodium N-ethylphenylsulfamate and 2,5-dichlorophenyldiazonium chloride. The diazonium solution was added to a thick suspension of sodium ethylphenylsulfamate. The sulfamate precipitate gradually began to dissolve, forming a brown color. A brown precipitate formed, but not of the usual coarse, lustrous plates, characteristic of diazo salts, but of fine crystals, combined as flakes. The filtered and washed brown precipitate was insoluble in water. When heated with α-naphthylamine in glacial acetic acid, the substance formed a dye, which is characteristic of diazoamino compounds.

Synthesis of 2-anthraquinonyldiazonium sulfamate. 2-Aminoanthraquinone was diazotized by Schaarschmidt's method [12]. Anthraquinonyldiazonium chloride was recrystallized from warm water.

0.02 mole of sodium sulfamate was dissolved in a few milliliters of cold water and several drops of acetic acid added to it. With vigorous stirring, a solution prepared from 0.018 mole of 2-anthraquinonyldiazonium chloride was added. A slightly yellow precipitate formed almost immediately and after a few minutes, it filled the reaction vessel. The precipitate was filtered off and recrystallized from 10% acetic acid, acidified with several drops of hydrochloric acid and heated to 50-60°. A small amount of an insoluble residue was filtered off and the filtrate cooled in ice. Coarse golden yellow crystals precipitated immediately and under a microscope, they appeated as elongated plates. The precipitate was filtered off, washed with water and ether and dried in vacuum, pressed out on a porous plate.

Found %: diazo nitrogen 7.97. $C_{14}H_9O_5N_3S \cdot H_2O$. Calculated %: diazo nitrogen 8.02.

Analysis for diazo component content. A sample of the material was dissolved in 100 ml of 5% acetic acid, acidified with a few drops of hydrochloric acid. To the solution was added excess of 0.05 N solution of β-naphthol in alkali, adjusted to pH 7 by the addition of acetic acid. The solution being analyzed was brought to pH 7 with sodium bicarbonate, stirred for half-an-hour and the excess β-naphthol titrated with 0.05 N p-nitrophenyldiazonium solution.

0.2360 g of substance: 13.29 ml of 0.05 N β-naphthol solution. $C_{14}H_9O_5N_3S \cdot H_2O$. Calculated: 13.52 ml of 0.05 N β-naphthol.

Analysis for sulfamic acid content. A sample of the substance was dissolved as above. 10 ml of 5 N hydrochloric acid was added to the solution, which was titrated with 0.1 N nitrite solution.

0.6472 g of substance: 18.16 ml of 0.1 N nitrite solution. $C_{14}H_9O_5N_3S \cdot H_2O$. Calculated: 18.52 ml of 0.1 N nitrite solution.

SUMMARY

1. The reaction of diazo compounds with sulfamic, benzylsulfamic and N-ethylphenylsulfamic acids in an acid medium was investigated. Diazonium salts of these sulfamic acids were prepared.

2. It was shown that the diazonium salts of sulfamic acid and its alkyl- and aralkyl derivatives are colorless or only slightly colored. A strong color is only inherent in diazonium arylsulfamates.

3. It was established that the color of diazonium arylsulfamates did not depend on intermolecular reactions and depended little on the hydrogen bond, which may exist between the terminal nitrogen of the diazonium cation and the hydrogen on the imino group of the arylsulfamic acid.

4. It is proposed that the reason for color in diazonium arylsulfamates is a salt bond of peculiar character, which is capable of transmitting a conjugation effect between the electron acceptor diazonium cation and the electron donor arylsulfamate anion.

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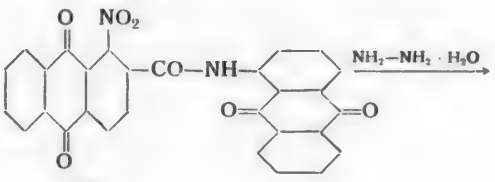
REACTION OF HYDRAZINE WITH NITRO COMPOUNDS OF THE ANTHRAQUINONE SERIES

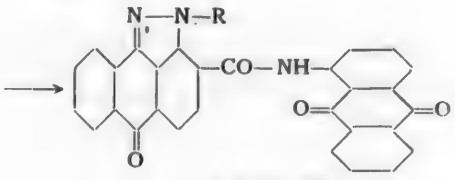
II. SYNTHESIS OF VAT DYES – DERIVATIVES OF PYRAZOLEANTHRONECARBOXYLIC ACID

N. S. Dokunikhin and I. D. Pletneva

The previous report [1] describes the formation of pyrazoleanthrone derivatives by hydrazine treatment of nitro compounds of the anthraquinone series, among them 1-nitroanthraquinone-2-carboxylic acid and its phenylamide. A further development of this work was the application of the procedure found to the synthesis of more complex materials, possessing the properties of vat dyes. The patent literature [2, 3] describes the (1'-anthraquinonyl)-amide of pyrazoleanthrone-2-carboxylic acid (I) as a yellow vat dye. We prepared this compound by treating the N-(1'-anthraquinonyl)-amide of 1-nitroanthraquinone-2-carboxylic acid (II) with hydrazine hydrate in pyridine and it was found to be the same as the product of acylating 1-aminoanthraquinone with the acid chloride of pyrazoleanthrone-2-carboxylic acid.



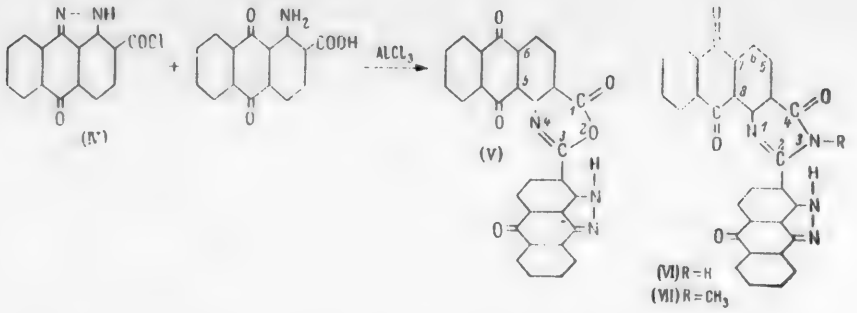
(II)



(I) R = H, (III) R=CH_3

Methylation of (I) gave an orange-yellow vat dye with structure (III).

New patents [4] describe the preparation of a series of vat dyes by the action of acid chlorides of substituted 2-anthraquinonecarboxylic acid in the presence of $FeCl_3$, $AlCl_3$ which, as a result of the simultaneous acylation and closing of the ring, gave derivatives of 5,6-phthaloyl-2,4,1-benzoxazine. When treated with ammonia and amines the latter readily exchanged the ring oxygen for nitrogen and were converted into the corresponding derivatives of 7,8-phthaloyl-3,4-dihydro-4-oxo-quinazoline [5]. On using the acid chloride of pyrazoleanthrone-2-carboxylic acid (IV) as an acylating agent one would expect a similar series of vat dyes with somewhat different shades. Treatment of 1-aminoanthraquinone-2-carboxylic acid with (IV) in the presence of $AlCl_3$ gave a compound which, according to analysis data, had structure (V) and when heated with aqueous ammonia exchanged oxygen for nitrogen to form substance (VI), that gave a vat dye coloring cellulose fibers dull yellow with a reddish tinge.



The corresponding compound (VII), prepared by using methylamine instead of ammonia, unexpectedly showed no affinity for cellulose fiber in contrast to similar derivatives of substituted anthraquinonecarboxylic acid that are vat dyes.

EXPERIMENTAL

3.85 g of the acid chloride of the 1-nitro-2-carboxylic acid of anthraquinone (m. p. 236-237°) was boiled in xylene with 2.32 g of 1-aminoanthraquinone (m. p. 250-251°) until the evolution of HCl ceased. The yield of the N-(1'-anthraquinonyl)-amide of the 1-nitro-2-carboxylic acid of anthraquinone (II) was 4.00 g.

Found %: N 5.72, 5.77. $C_{29}H_{14}O_7N_2$. Calculated %: N 5.58.

4.0 g of (II) and 10.0 g of hydrazine hydrate were boiled for 3 hrs in 40 ml of pyridine, diluted with water, filtered, washed free from pyridine and dried. The yield was 2.82 g of substance, which was dissolved in 25 ml of 90% H_2SO_4 and filtered through a glass filter and 6 ml of H_2O slowly added to the filtrate. The yellow rectangular prisms formed were filtered off, treated with warm water and again filtered, the acid washed off and the product dried to give 1.3 g of the N-(1'-anthraquinonyl)-amide of pyrazoleanthrone-2-carboxylic acid (I), which reacted with an alkaline solution of hydrosulfite to give a violet-black dye, coloring cellulose fibers a bright lemon yellow.

Found %: N 8.98, 9.15. $C_{29}H_{15}O_4N_3$. Calculated %: N 8.95. λmax_1 320 mμ, $\epsilon \cdot 10^{-4}$ 2.26; λmin 400 mμ, $\epsilon \cdot 10^{-4}$ 1.35; λmax_2 435 mμ, $\epsilon \cdot 10^{-4}$ 1.55 (the absorption spectrum of a water suspension of the dye was measured [6]).

2.64 g of pyrazoleanthrone-2-carboxylic acid was boiled in 20 ml of thionyl chloride (b. p. 75.5-76.5°) until a clear solution was formed. The thionyl chloride was distilled off and the residue, which consisted of yellow, hexagonal plates (IV), was treated with 30 ml of nitrobenzene and 2.23 g of 1-aminoanthraquinone (m. p. 250-251°). The mixture was heated at 150° until the vigorous evolution of hydrogen chloride ceased (about 36 hrs), filtered at 120°, washed and dried. The yield was 3.71 g. Reprecipitation from 33 ml of H_2SO_4 (90%) with 7.5 ml of H_2O (as described above) yielded 2.77 g of (I), which formed a violet-black hydrosulfite vat dye, coloring cellulose fibers lemon yellow.

Found %: N 8.83, 9.04. $C_{29}H_{15}O_4N_3$. Calculated %: N 8.95. λmax_1 320 mμ, $\epsilon \cdot 10^{-4}$ 2.22; λmax_2 400 mμ, $\epsilon \cdot 10^{-4}$ 1.38; λmax_3 435 mμ, $\epsilon \cdot 10^{-4}$ 1.54.

2.35 g of dye (I) and 0.6 g of KOH were heated in 30 ml of $C_6H_5NO_2$ to 100°, a solution of 3.8 g methyl p-toluenesulfonate in 10 ml of $C_6H_5NO_2$ added over a period of 3 hrs, the mixture heated at 130° for 7.5 hrs and another 0.6 g of KOH added, followed by 3.8 g of methyl p-toluenesulfonate, added over a period of 3 hrs. The mixture was stirred at 130° for a further 6 hrs. The mixture was cooled and the precipitate filtered off and washed with methyl alcohol and water to yield 0.79 g of dye (III), which gave a black-violet alkaline hydrosulfite vat dye, coloring cellulose fibers orange-yellow.

λmin 309 mμ, $\epsilon \cdot 10^{-4}$ 0.43; λmax 460 mμ, $\epsilon \cdot 10^{-4}$ 0.60. Found %: N 8.40, 8.56. $C_{30}H_{17}O_4N_3$. Calculated %: N 8.69.

The acid chloride of pyrazoleanthrone-2-carboxylic acid, prepared from 9.24 g (0.035 mole) of pyrozoleanthrone-2-carboxylic acid (see above), was treated with 100 ml of dry nitrobenzene, 2.10 g of anhydrous $AlCl_3$

and 9.4 g (0.035 mole) of the 1-amino-2-carboxylic acid of anthraquinone. The reaction mixture was heated with stirring under an air condenser, fitted with a calcium chloride tube, up to 150° over a period of 3 hrs and then at 150° for 10-12 hrs until the vigorous evolution of hydrogen chloride ceased. Towards the end of the reaction, a sample under a microscope showed, instead of the original yellow hexagonals of the acid chloride and the crimson amorphous particles of 1-amino-2-carboxylic acid of anthraquinone, red-brown platelets. The mass was filtered hot and washed with 20 ml of nitrobenzene and 100 ml of benzene; we obtained 10.35 g of 5,6-phthaloyl-2,4,1-benzoxazine-3-(2'-pyrazoleanthronyl) (V).

Found %: C 72.33, 72.23; H 2.73, 2.77; N 8.15, 8.25. $C_{30}H_{23}O_5N_3$. Calculated %: C 72.73; H 2.64; N 8.48.

(V) gave a red-brown vat dye with hydrosulfite and alkali, which weakly colored cellulose fibers a pale yellow.

5 g of (V) was heated in a tube with 30 ml of 25% ammonia at 130° for 5 hrs. The brown precipitate formed was transferred to a filter and washed with water until there was no reaction with brilliant yellow paper. We obtained 4.72 g of (VI), which formed a black-green vat dye with alkaline hydrosulfite, coloring cellulose fibers yellow with a reddish tinge.

Found %: N 10.97, 10.95. $C_{30}H_{14}O_4N_4$. Calculated %: N 11.33. λmax_1 310 mμ, $\epsilon \cdot 10^{-4}$ 4.09; λmax_2 320 mμ, $\epsilon \cdot 10^{-4}$ 4.16; λ_{min} 400 mμ, $\epsilon \cdot 10^{-4}$ 1.85; λmax_3 445 mμ, $\epsilon \cdot 10^{-4}$ 2.40.

2 g of (V) was heated in a tube with 40 ml of aqueous CH_3NH_2 solution (99 g of 1 liter) at 130° for 5 hrs. The precipitate was transferred to a filter and washed until there was no reaction to brilliant yellow paper. We obtained 1.88 g of 7,8-phthaloyl-3,4-dihydro-4-oxo-2-(2'-pyrazoleanthronyl)-quinazoline (VII), which dissolved when treated with hydrosulfite and NaOH solution. The leuco compound obtained in this way showed no affinity for cellulose fibers.

Found %: C 72.74, 72.73; H 2.99, 3.22; N 10.85, 10.83. $C_{31}H_{17}O_4N_4$. Calculated %: C 73.08; H 3.36; N 10.85.

SUMMARY

1. Treatment of the N-(1'-anthraquinonyl)-amide of the 1-nitro-2-carboxylic acid of anthraquinone with hydrazine hydrate gave the N-(1'-anthraquinonyl)-amide of pyrazoleanthrone-2-carboxylic acid.

2. The acid chloride of pyrazoleanthrone-2-carboxylic acid reacted with 1-aminoanthraquinone-2-carboxylic acid in the presence of $AlCl_3$ to give 5,6-phthaloyl-2,4,1-benzoxazine-3-(2'-pyrazoleanthronyl), which gave 7,8-phthaloyl-3,4-dihydro-4-oxo-2-(2'-pyrazoleanthronyl)-quinazoline and 7,8-phthaloyl-3,4-dihydro-4-oxo-3-methyl-2-(2'-pyrazoleanthronyl)-quinazoline with ammonia and methylamine.

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[1] N. S. Dokunikhin and I. D. Pletneva, J. Gen. Chem. 27, 791 (1957).*

[2] German Patent 540931 (1929); Frdl. 18, 1474.

[3] German Patent 542801 (1929); Frdl. 18, 1363.

[4] French Patent 847152 (1938); C. A. 35, 5719 (1941).

[5] British Patent 720795 (1954); C. A. 49, 9283B (1955).

[6] L. I. Belen'kii, Sci. Research Trans. Center Sci. Inst. Fiber Cotton Ind. (State Light Ind. Press, Moscow, 1954) 97. **

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** In Russian.

AZO DERIVATIVES OF CYANINE DYES

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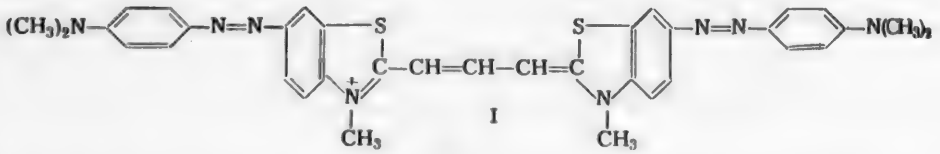
Cyanine dye analogs containing an azo group in the chromophore instead of a vinyl group have been described many times. They have been prepared, for example, by diazotizing 2-aminobenzthiazole derivatives and by coupling the diazo compounds obtained with active methyl or methylene groups of other nitrogen heterocycles [1]. However, typical cyanine dyes such as thiacarbocyanine (A) with arylazo groups as substituents in the benzene rings of the benzthiazole have not been prepared previously. Nevertheless, such dyes, which are simultaneously poly-

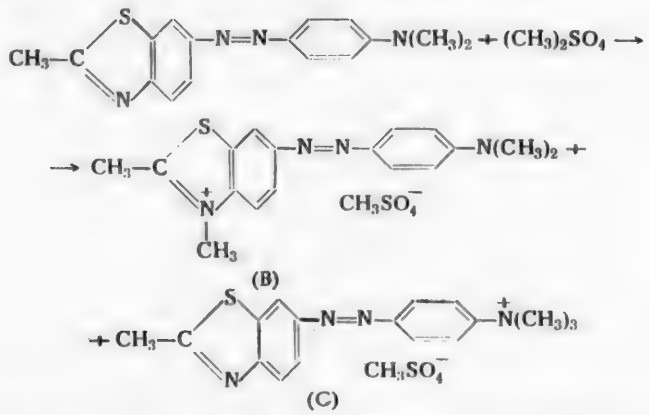


I

(A)

methine and azo dyes, are of definite value. They could explain whether an azo group together with a polymethine chain forms one common chromophore or whether the chromophores are, to a certain degree, disconnected here. It would also be valuable to determine the effect of the azo group on the sensitizing capacity of thiacyanines.

We synthesized a series of this type of dye, mainly thiacarbocyanines and styryls, starting with 2-methyl-5- and 2-methyl-6-arylazo derivatives of benzthiazole, whose preparation we recently described [2]. These bases were heated with dimethyl or diethyl sulfate and the quaternary salts obtained were condensed in the usual way to form cyanine dyes. One might expect that, in the case of dimethylaminophenylazo derivatives of 2-methylbenzthiazole, dimethyl sulfate molecules would be added not only to the nitrogen atom of the thiazole nucleus but also to the amine group to form two isomeric quaternary salts (B) and (C).



(B)

(C)

However, the quaternary salt we obtained was found to be capable of condensation to form styryls and carbocyanines and, consequently, was of structure (B) and not (C). In addition, if salt (C) was formed the effect of the

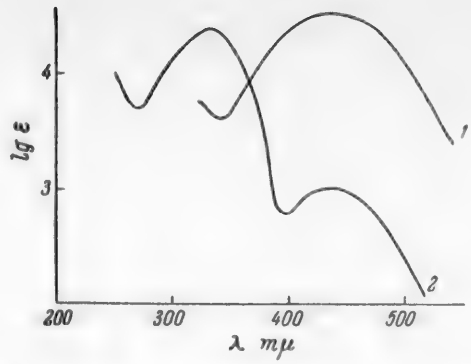


Fig. 1. Absorption spectra. 1) Methiodide of 2-methyl-6-p-dimethylaminophenylazobenzthiazole, 2) 2-methyl-6-phenylazobenzthiazole.

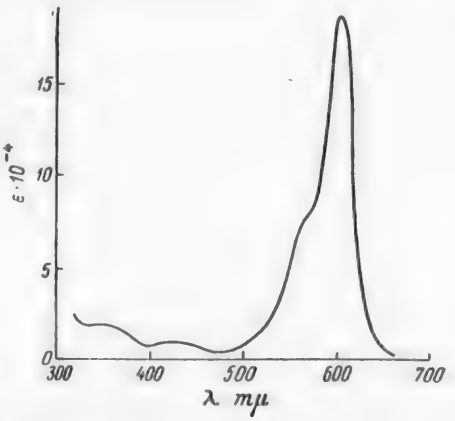


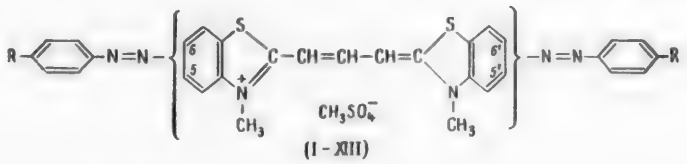
Fig. 2. Absorption spectrum of 3,3'-dimethyl-6,6'-di-(phenylazo)-thiacarboxyanine methyl sulfate.

amine group on light absorption would have been eliminated and the absorption curve of the salt would have approached the absorption curve of 2-methyl-6-phenylazobenzthiazole. Figure 1 shows that the substance we obtained differed a great deal in absorption from 2-methyl-6-phenylazobenzthiazole.

Due to the high molecular weight of the cyanine dyes prepared from the quaternary salts of 2-methylarylazo derivatives of benzthiazole, there were difficulties in purifying them. Even the methyl sulfates were difficultly soluble in the usual organic solvents. Therefore, the greater part of the dyes were purified not by crystallization but by boiling in alcohol and washing with hot alcohol and ether. As the analyses show, the preparations were purified sufficiently by this method.

The absorption curves of the dyes we prepared in alcohol solutions were determined on an SF-4 spectrophotometer. It was found that all the arylazothiacarbocyanines have one narrow and very intense absorption band, similar to the absorption band of unsubstituted thiacarbocyanine, but located in a much longer wavelength part of the spectrum. As an example, we give the absorption curve of one of the simplest dyes in this group – 6,6-diphenylazothiacarbocyanine (Fig. 2).

We see here one sharply expressed maximum at 610 mμ (ε 190500), consequently, both azo groups are conjugated with the polymethine chain, forming a common chromophore. Two weak absorption bands are also noticeable in the spectrum range from 320 to 480 mμ, with maxima at 350 mμ (ε 18,000) and 430 mμ (ε 7600). This section of the curve corresponds to the absorption of 2-methyl-6-phenylazobenzthiazole, which has the same two absorption bands – K-band with a maximum at 337 mμ and a weak R-band with a maximum at 435 mμ [2]. Thus, the absorption spectrum of a complex dye molecule has also partial chromophores which are characteristic of the corresponding aromatic azo compounds, and their bands are somewhat displaced towards the long wavelength section of the spectrum. The absorption curves of other symmetrical arylazocarbocyanines have a similar structure. Table 1 gives the absorption maxima and molecular extinctions of symmetrical arylazothiacarbocyanines (I-XIII) with the general formula



(I - XIII)

By comparing the absorption spectra of isomeric thiacarbocyanines, given in Table 1, which contain identical arylazo groups in positions 6,6' and 5,5', one may see that all 6,6' derivatives have absorption maxima that lie 30-38 mμ further towards the red end of the spectrum than those of 5,5' derivatives, with almost identical intensity of absorption. This interesting rule shows that the azo group is conjugated more readily with the polymethine chromophore through the nitrogen atom of the thiazole nucleus than through the sulfur atom. No such difference exists between the thiacarbocyanines containing simpler polar groups in positions 6,6' and 5,5'. Replace-

TABLE 1

Dye	R	Position of arylazo groups	Absorption maximum (in mμ)	log ε
(I)	H	6,6'	610	5.27
(II)	H	5,5'	580	5.27
(III)	OCH_3	6,6'	612	5.19
(IV)	OCH_3	5,5'	580	5.16
(V)	OH	6,6'	614	4.82
(VI)	OH	5,5'	580	4.84
(VII)	$OCOCH_3$	6,6'	607	4.80
(VIII)	$OCOCH_3$	5,5'	574	4.83
(IX *)	$N(CH_3)_2$	6,6'	635	4.78
(X **)	$N(CH_3)_2$	5,5'	597	4.82
(XI)	$NHCOCH_3$	6,6'	618	4.79
(XII)	SCH_3	6,6'	618	4.83
(XIII)	NO_2	6,6'	625	4.65

* Perchlorate.

** Iodide.

ment of the hydrogen atoms in positions 6,6' and 5,5' of a thiacarbocyanine by amino groups also displaces the absorption maximum by 40 mμ towards the long wavelength section of the spectrum. Methoxy and hydroxy groups also affect thiacarbocyanine absorption in the same way, whether they are introduced into positions 6,6' or 5,5'. Only 6,6'-dinitrothiacarbocyanine (absorption maximum at 585 mμ) has a deeper color than 5,5'-dinitrothiacarbocyanine (absorption maximum at 560 mμ). In indocarbocyanines (D), where the substituent may be conjugated with

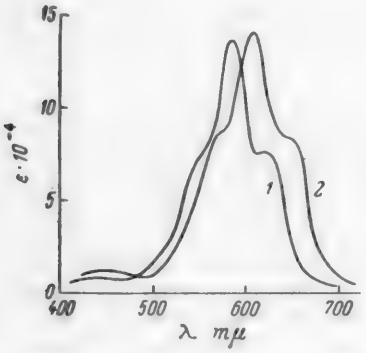
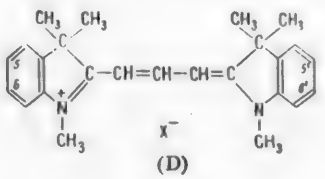


Fig. 3. Absorption spectra. 1) Biscyanine (XIX), 2) biscyanine (XX).

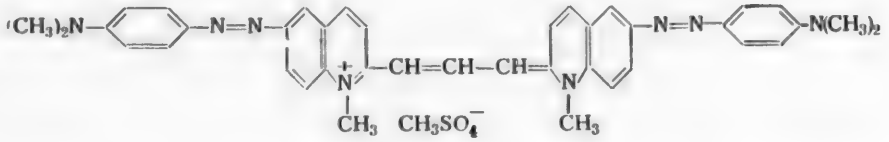


(D)

the chain only through a nitrogen atom, the dimethylamino groups in positions 5,5' displace the absorption maximum 60 mμ towards the long wavelength section of the spectrum and in positions 6,6' – only by 23 mμ [3].

Among the symmetrical bisarylazothiacarbocyanines we prepared mesoethyl substituted dyes (I) (XIV, λ_{max} 605 mμ, log ε 4.82) and dyes (VI) (XV, λ_{max} 570 mμ, log ε 4.90). As usual, their absorption maxima are somewhat displaced towards the short wavelength section of the spectrum.

One quinocarbocyanine (XVI) was also synthesized.

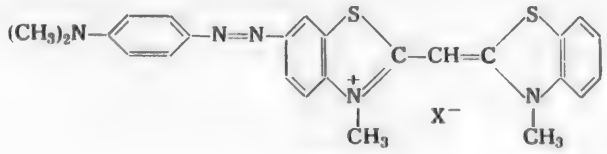


(XVI)

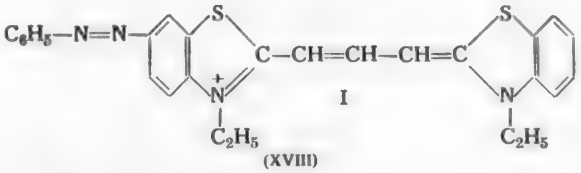
Its color is much deeper and more intense (λ_{max} 670 mμ, log ε 5.28) than that of the thiacarbocyanines (IX) corresponding to it and like the majority of quinocyanines it has a second shorter wavelength absorption maximum (λ_{max} 625 mμ, log ε 4.98).

The unsymmetrical monomethinecyanine (XVII) we synthesized has, in addition to the main absorption maximum at 490 mμ (log ε 4.85), a second, less intense maximum at 420 mμ (log ε 4.44), which probably corresponds to the absorption maximum of monomethinecyanine (422 mμ).

The absorption maximum of the unsymmetrical thiacarbocyanine (XVIII) we prepared lies at 580 mμ (log ε 4.90). This is 4 mμ less than the additive value; consequently, the phenylazo group quite strongly lowers the basicity of the benzthiazole nucleus to which it is connected.

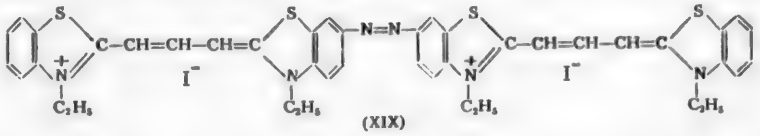


(XVII)



(XVIII)

The diquaternary salt of 2,2'-dimethyl-6,6'-azobenzthiazole and the ethiodide of 2- ω-acetanilidovinylbenzthiazole gave the biscyanine (XIX) with a very unusual absorption curve (Fig. 3, curve 1). The most intense maximum is not the one with the longest wavelength (λ_{max} 620 mμ, log ε 4.89), but the one next to it towards



(XIX)

shorter wavelengths (λ_{max} 588 mμ, log ε 5.14). Apparently, the long wavelength band corresponds to the absorption of the conjugation chain, which passes through the whole dye molecule and the next, more intense band corresponds to the absorption of that part of the molecule which includes thiacarbocyanine with one azo group (see dye XVIII). A similar absorption band (λ_{1max} 640-665 mμ, log ϵ_1 4.94, λ_{2}max 610 mμ, log ϵ_2 5.15, λ_{3}max 570 mμ, log ϵ_3 4.93) is found in the case of the biscyanine (XX), which was prepared from the same azobenzthiazole and the ethiodide of 2-ω-acetanilidovinylquinoline (Fig. 3, curve 2).

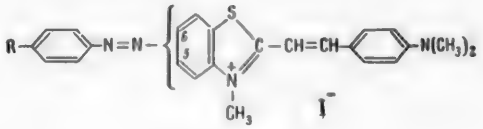
TABLE 2

Dye	R	Position of azo group	Absorption maximum (in mμ)	log ε
(XXI)	H	6	560	4.81
(XXII)	OCH_3	6	560	4.77
(XXIII *)	$OCOCH_3$	6	565	4.82
(XXIV)	SCH_3	6	565	4.86
(XXV **)	$N(CH_3)_2$	6	573	4.79
(XXVI)	$N(CH_3)_2$	5	553	4.78

* Perchlorate.

** Methyl sulfate.

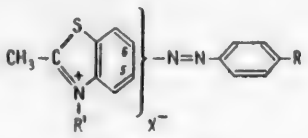
The different effect on light absorption of arylazo groups in positions 5 and 6 of the benzthiazole nucleus was observed not only in the appropriate carbocyanines but also in styryl dyes. Table 2 gives the absorption maxima and the molecular extinctions of styryls (XXI-XXVI) with the general formula as seen below



(XXI - XXVI)

EXPERIMENTAL

Quaternary salts. All the quaternary salts, used as starting materials in the synthesis of dyes, were prepared by heating 2-methyl-5- or 2-methyl-6-arylazo derivatives of benzthiazole, which we described previously [2], on a water bath with 1.5 mole of dimethyl sulfate or diethyl sulfate in benzene solution. For purification and analysis, the methyl and ethyl sulfates obtained were boiled with active charcoal in aqueous solution and precipitated with potassium iodide or sodium perchlorate in the form of the iodides or perchlorates, which were recrystallized from water. The dyes were prepared from unpurified alkyl sulfates. In Table 3 are given the conditions of preparation and melting points (uncorrected) of the quaternary salts (XXVII-XL) of the general formula



(XXVII - XL)

TABLE 3

Quaternary salts	R	R'	X	Position of azo group	Length of heating (in min)	Yield (in %)	Melting point (decomp.)
(XXVII)	H	CH_3	I	6	60	47	226—227°
(XXVIII)	H	C_2H_5	I	6	30 *	29	232—233
(XXIX)	H	CH_3	I	5	60	61	198
(XXX)	OH	C_2H_5	ClO_4	6	25 *	17	214—215
(XXXI)	OH	CH_3	I	5	60 **	45	215
(XXXII)	OCH_3	CH_3	I	6	60	34	220—221
(XXXIII)	OCH_3	C_2H_5	I	6	40 *	29	205—206
(XXXIV)	OCH_3	CH_3	I	5	60	30	224
(XXXV)	$N(CH_3)_2$	CH_3	ClO_4	6	60	66	220
(XXXVI)	$N(CH_3)_2$	CH_3	I	5	60	39	163
(XXXVII)	NO_2	CH_3	ClO_4	6	60	33	240—241
(XXXVIII)	$NHCOCH_3$	CH_3	I	6	60	33	231—233
(XXXIX)	SCH_3	CH_3	I	6	60	54	218—219
(XL)	Cl	CH_3	ClO_4	6	60	60	238

* At 120° without solvent.

** At 100° in nitrobenzene.

The methiodide of 6-p-dimethylaminophenylazoquinaldine (XLI) was prepared similarly. The yield was 43% and the m. p. 218° (with decomp.).

The diethiodide of 2,2'-dimethyl-6,6'-azobenzthiazole (XLII) was prepared by heating the base with 3 moles of dimethyl sulfate for 40 min at 120°. The iodide, prepared by adding potassium iodide to the aqueous solution, was recrystallized twice from water. The yield was 90% of orange needles with m. p. 236-237° (with decomp.). The results of analyzing the salts listed are given in Table 4.

Dyes. The symmetrical carbocyanines were prepared by the usual method. 0.2-0.4 g of the quaternary salt (for the most part unrecrystallized methyl sulfate) in 3-5 ml of dry pyridine was boiled under reflux with 4 moles of orthoformic ester. The mixture was cooled and the precipitated dye filtered off, washed with alcohol and ether and recrystallized. The dyes which were difficultly soluble in alcohol, were simply purified by washing with boiling alcohol and ether. The conditions of preparation, yields and melting points of the symmetrical carbocyanines are given in Table 5.

TABLE 4

Quaternary salts	Empirical formula	N (%) found	N (%) calc.
(XXVII)	$C_{15}H_{14}N_3SI$ *	10.54, 10.53	10.63
(XXVIII)	$C_{16}H_{16}N_3SI$	10.17, 10.21	10.27
(XXIX)	$C_{15}H_{14}N_3SI$	10.60, 10.57	10.63
(XXX)	$C_{16}H_{16}O_5N_3SCl$	10.35, 10.47	10.58
(XXXI)	$C_{15}H_{14}ON_3SI$ **	10.33, 10.30	10.22
(XXXII)	$C_{16}H_{16}ON_3SI$ ***	9.81, 9.76	9.88
(XXXIII)	$C_{17}H_{18}ON_3SI$	9.22, 9.29	9.56
(XXXIV)	$C_{16}H_{16}ON_3SI$	9.74, 9.70	9.88
(XXXV)	$C_{17}H_{15}O_4N_3SCl$	13.72, 13.77	13.66
(XXXVI)	$C_{17}H_{19}N_4SI$ ****	12.89, 12.73	12.78
(XXXVII)	$C_{15}H_{13}O_6N_4SCl$	13.71, 13.89	13.53
(XXXVIII)	$C_{17}H_{17}ON_4SI$	12.26, 12.14	12.39
(XXXIX)	$C_{16}H_{16}N_3S_2I$	9.39, 9.34	9.52
(XL)	$C_{15}H_{13}O_4N_3SCl_2$	10.32, 10.41	10.45
(XLI)	$C_{19}H_{21}N_4I$	12.72, 12.82	12.96
(XLII)	$C_{20}H_{22}N_4S_2I_2$	8.54, 8.78	8.80

* Found %: I 32.16, 32.18. Calculated %: I 32.15.

** Found %: I 30.33, 30.34. Calculated %: I 30.94.

*** Found %: I 29.85, 29.69. Calculated %: I 29.88.

**** Found %: I 29.05, 29.19. Calculated %: I 28.99.

TABLE 5

Dyes (see Table 1)	Quaternary salts (see Table 3)	Length of boiling (in min)	Crystallization solvent	Yield (in %)	Melting point (decomp.)	External appearance of dye
(I)	(XXVII *)	20	Alcohol	44	265—266°	Blue needles
(II)	(XXIX *)	25	Alcohol	64	283	Violet needles with a metallic luster
(III)	(XXXII *)	20	CH_3OH	58	240	Prisms with a metallic luster
(IV)	(XXXIV *)	20	CH_3OH	34	243	Violet powder
(V)	(XXX)	20	CH_3OH	37	217—218	Dark blue powder
(VI)	(XXXI *)	25	—	34	251	Violet powder
(VII)	(XXX)	20 ***	CH_3OH	42	237—238	Dark blue powder
(VIII)	(XXXI *)	25 ***	—	28	289—290	Violet powder
(IX)	(XXXV)	25	—	59	249—250	Green needles
(X)	(XXXVI)	20	—	23	253—254	Blue crystals
(XI)	(XXXVIII *)	25 ****	—	46	254	Green needles
(XII)	(XXXIX *)	30	—	50	259—260	Green needles
(XIII)	(XXXVII *)	40	Nitrobenzene	65	267—268	Dark powder
(XIV)	(XXVIII)	20 **	Alcohol	42	222	Blue needles
(XV)	(XXXI *)	20 **	Alcohol	15	226	Violet powder
(XVI)	(XLII)	20	—	42	246	Green needles

* Methyl sulfate.

** Orthopropionic ester was used instead of orthoformic.

*** The solvent was acetic anhydride.

**** The solvent was a mixture of pyridine and acetic anhydride.

The unsymmetrical carbocyanine (XVIII) was prepared by boiling a mixture of 0.1 g of 2-methyl-6-phenylazobenzthiazole ethiodide, 0.1 g of 2-ω-acetanilidovinylbenzthiazole ethiodide, 0.05 g of anhydrous sodium acetate and 2 ml of acetic anhydride for 20 min. When the substance had been crystallized from alcohol, the yield was 0.07 g (50%) and the m. p. 237-238° (with decomp.).

TABLE 6

Dyes (see Table 2)	Quaternary salts (see Table 3)	Crystallization solvent	Yield (in %)	Melting point (decomp.)	External appearance of dye
(XXI)	(XXVII)	—	77	243—244°	Green needles
(XXII)	(XXXII *)	—	42	225—226	Green prisms
(XXIII)	(XXX **)	—	37	268—269	Green prisms
(XXIV)	(XXXIX *)	CH_3OH	54	234—235	Green prisms
(XXV)	(XXXV)	Alcohol	48	206	Dark blue powder
(XXVI)	(XXXVI *)	CH_3OH	40	216	Violet powder

* Iodide.

** Perchlorate.

For the synthesis of the monomethinecyanine (XVII), we boiled a mixture of 0.32 g of 2-methyl-6-p-diaminophenylazobenzthiazole methylmethyl sulfate, 0.16 g of anhydrous sodium acetate and 0.25 g of 2-methylmercaptobenzthiazole methyl methyl sulfate in 6 ml of anhydrous alcohol for 1 hr. For purification, the dye was chromatographed in a chloroform solution on aluminum oxide. After extracting with boiling alcohol, we obtained 0.11 g (25%) of dark red needles with m. p. 264° (with decomp.).

The bisthiacarbocyanine (XIX) was synthesized from 0.3 g of 2,2'-dimethyl-6,6'-azobenzthiazole diethiodide and 0.41 g of 2-ω-acetanilidovinylbenzthiazole ethiodide, which were heated in acetic anhydride with anhydrous sodium acetate. When recrystallized from alcohol, it formed a dark blue powder. The yield was 0.21 g (44%) and the m. p. 150-152° (with decomp.).

Similarly, from the same diquaternary salt and 2-ω-acetanilidovinylquinoline ethiodide we obtained a 39% yield of the bisthiaquinocarbocyanine (XX) as a dark blue powder with m. p. 228° (with decomp.).

TABLE 7

Dyes	Empirical formula	N (%) found	N (%) calculated
(I)	$C_{32}H_{28}O_4N_6S_3$	12.65, 12.95	12.80
(II)	$C_{32}H_{28}O_4N_6S_3$	12.68, 12.79	12.80
(III)	$C_{31}H_{32}O_6N_6S_3$	11.69, 11.67	11.73
(IV)	$C_{31}H_{32}O_6N_6S_3$	11.52, 11 64	11.73
(V)	$C_{32}H_{28}O_6N_6S_3$	12.15, 12.12	12.21
(VI)	$C_{32}H_{28}O_6N_6S_3$	12.37, 12.30	12.21
(VII)	$C_{36}H_{32}O_8N_6S_3$	10.74, 10.69	10.88
(VIII)	$C_{36}H_{32}O_8N_6S_3$	10.71, 10.77	10.88
(IX)	$C_{35}H_{35}O_4N_8S_2Cl$	15.08, 15.16	15.34
(X)	$C_{35}H_{35}N_8S_2I$	14.50, 14.61	14.78
(XI)	$C_{36}H_{34}O_6N_8S_3$	14.28, 14.34	14.54
(XII)	$C_{34}H_{32}O_4N_6S_5$	11.16, 11.14	11.23
(XIII)	$C_{32}H_{26}O_4N_8S_3$	14.72, 14.61	15.01
(XIV)	$C_{35}H_{33}N_6S_2I$	11.60, 11.49	11.54
(XV)	$C_{34}H_{32}O_6N_6S_3$	11.69, 11.70	11.73
(XVI)	$C_{40}H_{32}O_4N_8S$	15.43, 15.36	15.34
(XVII)	$C_{26}H_{27}O_4N_5S_3$	12.39, 12.28	12.30
(XVIII)	$C_{27}H_{25}N_4S_2I$	9.34, 9.30	9.40
(XIX)	$C_{42}H_{40}N_6S_4I_2$	8.21, 8.25	8.32
(XX ***)	$C_{46}H_{44}N_6S_2I_2$	8.34, 8.37	8.42
(XXI)	$C_{24}H_{23}N_4SI$	10.53, 10.57	10.64
(XXII)	$C_{25}H_{25}ON_3SI$	10.22, 10.29	10.07
(XXIII)	$C_{26}H_{25}O_6N_4SCl$	9.86, 10.01	10.07
(XXIV)	$C_{25}H_{25}N_4S_2I$	9.64, 9.57	9.79
(XXV)	$C_{27}H_{31}O_4N_5S_2$	12.48, 12.57	12.66
(XXVI)	$C_{26}H_{28}N_5SI$	12.22, 12.28	12.30

* Found %: I 25.26, 25.07. Calculated %: I 25.45.

All the styryl dyes, listed in Table 2, were synthesized from the appropriate quaternary salts by boiling them in acetic anhydride with an equivalent amount of p-dimethylaminobenzaldehyde for 20 min. The precipitate of dye was crystallized from alcohol or washed with boiling alcohol and ether. The preparation conditions of various styryl dyes and some of their properties are given in Table 6.

Table 7 gives the analysis results for all the dyes described in this work.

SUMMARY

The quaternary salts of 2-methyl-5- and 2-methyl-6-arylazobenzthiazoles gave a series of symmetrical and unsymmetrical thiacyanines and styryls, containing arylazo groups as substituents in the benzene rings. It was found that the absorption spectra of these dyes had one intense absorption band. Consequently, the azo group and polymethine chain form one common chromophore. The absorption bands of 6-arylazo derivatives of thiacyanines are displaced considerably towards the red end of the spectrum in comparison with those of the 5-arylazo derivatives.

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THE REACTION OF HYDRAZINE WITH CARBON DISULFIDE

EXPERIMENTS ON THE SYNTHESIS OF DIISOTHIOCYANOGEN

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Previously, one of us had shown that under certain conditions alkylene diisothiocyanates may be prepared using a modified Calus method [1]. It seemed interesting to use a similar method for preparing the simplest representative of this series of compounds – diisothiocyanogen SCN–NCS, which was previously unknown. The scheme for such a synthesis may be represented by the following equations

$$NH_2NH_2 + 2CS_2 + 2NaOH \longrightarrow \underset{(I)}{(NHCSSNa)_2} \quad (1)$$

$$(NHCSSNa)_2 + 2ClCOOC_2H_5 \longrightarrow \underset{(II)}{(NHCSSCOOC_2H_5)_2} \quad (2)$$

$$(NHCSSCO_2C_2H_5)_2 \xrightarrow{\text{pyrolysis}} \underset{(III)}{(NCS)_2} + 2COS + 2C_2H_5OH \quad (3)$$

Hydrazine reacted with carbon disulfide (excess) by Busch's method, to form 1,5-dithiol-1,3,4-thiadiazole and not hydrazinebisdithiocarbonic acid.

$$NH_2NH_2 + 2CS_2 \longrightarrow HS{-}\underset{\displaystyle S}{\overset{\displaystyle N{=}C}{\overset{\displaystyle N{=}C}{}}}{-}SH + H_2S$$

Hydrazinebisdithiocarbonic acid derivatives were prepared by the reaction of hydrazine with potassium thiocyanate (diamide) [3] or with diethyl trithiocarbonate (diethyl ester) [4].

$$HSCN + NH_2NH_2 \longrightarrow (NHCSNH_2)_2$$

$$SC(SC_2H_5)_2 + NH_2NH_2 \longrightarrow (NHCS_2C_2H_5)_2 + C_2H_5SH$$

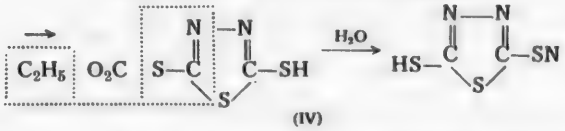
Hydrazinebisdithiocarbonic acid itself or its salts had not been prepared previously.

It was found that the sodium salt of this acid (I) was readily prepared by reacting hydrazine (1 mole) with carbon disulfide (2 moles) in the presence of sodium hydroxide (2 moles) in an aqueous medium and precipitating the salt with acetone from the solution thus formed (equation 1). The disodium salt thus obtained rapidly decomposed when heated and stored in air: however, it could be kept for weeks at a low temperature. Addition of silver or lead nitrate to the aqueous salt solution precipitated the silver or lead salts of the acid, which were difficultly soluble in water. The former was relatively stable and could be analyzed.

Thus, the first stage of the proposed synthesis was achieved without any special difficulties. The next stage also presented no difficulties – the preparation of the mixed dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids (II) (equation 2). Disodium salt (I) reacted with ethyl chloroformate in an aqueous medium to give a poor yield of (II), apparently because of the instability of the salt in an aqueous solution; this compound was prepared in better yield in a benzene or ether medium. In contrast to the salt of hydrazinebisdithiocarbonic acid, its dianhydride derivative was stable and could be recrystallized.

The last stage of the synthesis planned was carried out by pyrolyzing dianhydride (II) at 140-150° in vacuum. However, instead of the expected diisothiocyanogen (III) (or its polymer) we obtained an oily substance with b. p. 143-145° (1 mm) which did not contain an isothiocyanate group. The presence of an ethoxyl group in this product and its hydrolysis with 15% hydrochloric acid to a crystalline compound with m. p. 167° and other properties, which correspond to Busch's 2,5-dithiol-1,3,4-thiadiazole [2] indicated that the substance obtained had the structure of 2,5-dithiol-1,3,4-thiadiazole ethylcarbonate (IV). Its formation, apparently, occurred by the scheme

$$(NHCSSCO_2C_2H_5)_2 \longrightarrow [S{=}C{=}N{-}NH{-}CSSCO_2C_2H_5 \rightleftarrows$$
$$\rightleftarrows S{=}C{=}N{-}N{=}C(SH)SCO_2C_2H_5]$$



(IV)

The ease of such a cyclization with the formation of 1,3,4-thiadiazole derivatives was noted earlier using samples of the diamide and diethyl ester of hydrazinebisdithiocarbonic acid [3, 4]. Pyrolysis of dianhydride (II) under more drastic conditions at 250° also did not produce diisothiocyanogen. The main reaction product in this case, besides the tarry residue, was ethyl thiocyanate. The formation of ethyl thiocyanate may be explained by the thermal decomposition of the ester of the thiadiazole derivative (IV), which formed, apparently, as an intermediate product in this reaction (shown in the scheme by a dotted line). This observation and the hypothetical scheme of ethyl thiocyanate formation indicate that thiocyanates could possibly be obtained in other cases of the thermal decomposition of compounds containing $RO_2C{-}SCN$ groups.

The thermal decomposition of methyl and ethyl esters of thiocyanocarbonic acid, which we investigated in connection with the above, confirmed this hypothesis; in both cases the corresponding alkyl thiocyanates were obtained in yields of 50-60% of the theoretical.

$$ROCOSCN \longrightarrow CO_2 + RSCN$$

In order to avoid cyclization which occurred when dianhydride (II) was heated during the preparation of diisothiocyanogen, we decided to synthesize the analogous, less stable compound – the dianhydride of hydrazinebisdithiocarbonic and chlorocarbonic acids (V), during whose decomposition we might also expect the formation of diisothiocyanogen.

$$(NHCS_2Na)_2 + 2COCl_2 \xrightarrow{-2NaCl} (NHCS_2COCl)_2 \underset{-COS}{\overset{-2HCl}{\rightleftarrows}} (NCS)_2$$

(V)

Actually, material (V), hygroscopic yellow crystals, formed by reacting phosgene with the disodium salt of hydrazinedithiocarbonic acid, was unstable at room temperature, but in the absence of moisture could be kept at low temperatures (from −70° to −80°). Its composition was as expected; however, no diisothiocyanogen was formed when it decomposed at room temperature and under other conditions (in the presence of bases to bind the HCl). Thus, the two methods planned for synthesizing diisothiocyanogen did not give positive results.

Several attempts have been made to prepare materials analogous to diisothiocyanogen. Thus, at various times, Nef, Tiele and Staudinger tried to synthesize diisocyanogen $OCN{-}NCO$ [6], diisonitrile $CN{-}NC$ [5] and cyanocarbylamine $NC{-}NC$ [7] but were unsuccessful. It remains to be clarified to what degree all these failures, including ours, are due to the use of unsuitable methods for preparing this type of compound. It is possible that the materials named are not formed due to their extreme instability, which precludes the existence of these compounds, in contrast to such known pseudo-halogens as dicyanogen and dithiocyanogen.

EXPERIMENTAL

1. The reaction of hydrazine with carbon disulfide. Preparation of salts of hydrazinebisdithiocarbonic acid $(NHCS_2Me)_2$. With vigorous stirring, a solution of 6 g of hydrazine hydrate in 10 ml of water was added dropwise to a mixture of 16 g of freshly distilled carbon disulfide and 16 ml of 50% aqueous sodium hydroxide. The tem-

perature of the reaction mixture rose to 45° and then fell to room temperature. The orange-yellow solution obtained was kept for a further 30 min at 40°, then cooled in ice and salt and treated with cold acetone until the oil (lower layer) was completely precipitated. Seed crystals of the disodium salt of hydrazinebisdithiocarbonic acid were added to the cooled mass and then the lower layer was triturated until friable crystals formed and these were separated, washed with acetone and dried in vacuum. (The seed was prepared by triturating 0.5 ml of liquid from the lower layer with several portions of acetone with cooling in a carbon dioxide mixture.) We obtained 23 g of colorless crystals of the disodium salt.

0.5 g of the crystals were dissolved in 5 ml of cold water and mixed with a concentrated solution of $AgNO_3$. 0.7 g of the disilver salt was precipitated.

Found %: C 5.87, 5.61; N 6.58, 6.44; S 32.12, 31.91. $C_2H_2N_2S_4Ag_2$. Calculated %: C 6.03; N 7.03; S 32.2.

2. Preparation of the dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids (II). With stirring, 16 g of ethyl chloroformate was added dropwise to a mixture of 15 g of disodium hydrazinebisdithiocarbonate and 70 ml of dry ether at such a rate that there was a slow rise in the temperature of the reaction mixture to 40°. When all the ethyl chloroformate had been added, the flask was kept at 50° for 2 hrs. The precipitate of sodium chloride formed was separated and the filtrate evaporated in vacuum. We obtained 12.5 g of crystals, which were freed from the oil covering them by dissolution in chloroform and reprecipitation with ether (4-fold dilution), while cooled with carbon dioxide. Subsequent recrystallization from alcohol yielded colorless needles with m. p. 87°.

Found %: C 30.31, 30.24; H 3.58, 3.52; N 8.84, 8.75; S 38.66; OC_2H_5 26.96, 26.85. M 313 (in benzene). $C_8H_{12}O_4N_2S_4$. Calculated %: C 29.2; H 3.67; N 8.5; S 39.6; OC_2H_5 27.4. M 327.

3. Thermal decomposition of the dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids. Preparation of 2,5-dithiol-1,3,4-thiadiazole ethylcarbonate (IV). 3 g of the dianhydride (II) was heated at 140-150° for 30 min. The oil formed was vacuum distilled. We obtained 2 g of a colorless oil with an ester smell and b. p. 143-145° (2 mm), d^{20}_{20} 1.299.

Found %: OC_2H_5 19.93, 19.34. M 212.5 (in benzene). $C_5H_6O_2N_2S_3$. Calculated %: OC_2H_5 20.3. M 222.

0.5 g of the substance was heated at 100° for 5 hrs in an ampule with 5 ml of 15% hydrochloric acid. The oil crystallized on cooling. The crystals were pressed out on a porous plate and recrystallized from ether with carbon dioxide cooling. We obtained needles with m. p. 167° and other properties corresponding to 2,5-dithiol-1,3,4-thiadiazole [2].

4. Pyrolysis of dithiolthiadiazole ethylcarbonate (IV). 8 g of the ethylcarbonate with b. p. 143-145° (2 mm) was placed in a distillation flask and heated with a burner for 30 min. In the receiver we collected 3.2 g of a colorless liquid, distilling in the range 100-160°. The residue in the flask was carbonized. A second distillation yielded a fraction with b. p. 140-143° (1.5 g), d^{20}_{20} 1.005, $n^{20}D$ 1.4670, with the characteristic smell and properties of ethyl thiocyanate (see below for its constants).

Found %: C 40.87; H 5.64; N 15.15. M 83.5. C_3H_5NS. Calculated %: C 41.4; H 5.75; N 16.1. M 87.

5. Pyrolysis of ethyl thiocyanocarbonate. Preparation of ethyl thiocyanate. 5 g of ethyl thiocyanocarbonate with b. p. 83-85° (30 mm), prepared by Dixon and Teylor's method [8], was boiled under reflux for 2 hrs. The substance darkened and carbon dioxide was evolved. The tarry residue was distilled on a semimicrocolumn (6 theoretical plates). A fraction with b. p. 141-143° (2.0 g) had d^{20}_{20} 1.007, $n^{20}D$ 1.4675 and was identified as ethyl thiocyanate. The yield of ethyl thiocyanate was 60%. (According to literature data: b. p. 143.6°, $d^{22.9}_4$ 1.0071, $n^{22.9}D$ 1.4684 [9]).

Found %: N 15.73. M 84.3. C_3H_5NS. Calculated %: N 16.1. M 87.0.

6. Pyrolysis of methyl thiocyanocarbonate. Preparation of methyl thiocyanate. 5 g of methyl thiocyanocarbonate with b. p. 30° (12 mm), prepared by Dixon and Teylor's method [8], was treated as described in Expt. 5. We isolated 1.7 g of a colorless liquid with b. p. 132-133°, d^{20}_{20} 1.0730, $n^{20}D$ 1.4725, which was methyl thiocyanate. The yield was 55% of the theoretical. (According to literature data: b. p. 131°, d^{15}_4 1.0765, $n^{15}D$ 1.4745 [9]).

Found %: N 18.87. M 70.5. C_2H_3NS. Calculated %: N 19.2. M 73.0.

7. Reaction of disodium hydrazinebisdithiocarbonate with phosgene. A cooled solution of 21 g of phosgene in 100 ml of chloroform was added to a suspension of 10 g of the disodium salt in 50 ml of chloroform, which was stirred at a temperature of −5 to −6°. After 10 hrs, the sodium chloride was separated and the solvent evaporated in vacuum (all operations with the exclusion of moisture). We isolated 5.5 g of yellow hygroscopic crystals with the chracteristic smell of phosgene. The substance was unstable and decomposed in air forming a coarse orange powder with decomp. p. 100° and which was insoluble in water and the usual solvents.

Found %: C 15.95; N 10.71; Cl 23.51; S 39.98. M 297 (in benzene). $C_4H_2O_2N_2S_4Cl_2$. Calculated %: C 15.5; N 9.1; Cl 23.0; S 41.5. M 309.

1.2 g of the substance was mixed with 3 ml of aniline. The hydrochloride and excess aniline were washed out with 5% hydrochloric acid. The insoluble part (0.6 g) was recrystallized from alcohol. We obtained prisms with m. p. 237°. A mixed melting point with symmetrical diphenylurea was not depressed.

SUMMARY

1. Reaction of hydrazine with carbon disulfide in an aqueous-alkaline medium gave the disodium salt of hydrazinebisdithiocarbonic acid. This salt reacted with chlorocarbonic ester and phosgene to form the corresponding dianhydrides $(NHCS_2CO_2C_2H_5)_2$ and $(NHCS_2COCl)_2$.

2. When heated to 150° the dianhydride of hydrazinebisdithiocarbonic and ethylcarbonic acids was converted into 2,5-dithiol-1,3,4-thiadiazole ethylcarbonate, which at 250° split to form ethyl thiocyanate. This did not give diisothiocyanogen. Diisothiocyanogen was also not obtained by decomposition of the dianhydride of hydrazinebisdithiocarbonic and chlorocarbonic acids.

3. It was shown that alkylthiocyanocarbonic esters decompose when heated, to form alkyl thiocyanates.

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A METHOD OF OBTAINING FLUORINE DERIVATIVES OF SILICON, TIN, AND SULFUR

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Among metalloorganic compounds methods are known for replacing alkoxyl groups on the metal with chlorine by the action of inorganic or organic acid chlorides. The possible analogous replacement of alkoxyl groups with fluorine by a reaction with organic acid fluorides has not yet been specifically studied. It appeared interesting to us to study this reaction in alkoxyl derivatives of silicon, tin, and sulfur.

As we have shown, the fluorides of carboxylic acids, and especially the easily obtained acetyl fluoride, react with alkoxyl derivatives of these elements, transforming them into the corresponding fluorides by the general scheme

$$R_mEl(OR')_{n-m} + CH_3COF \rightarrow R_mEl(OR')_{n-m-1}F + CH_3COOR' .$$

This reaction goes easily when the central atom bound to the alkoxyl group is an electropositive element. Thus, alkoxy tin derivatives in the reaction with acetyl fluoride exchange their alkoxyl groups for fluorine even in the cold. In the case of compounds of silicon and sulfur the exchange occurs with heating. In all cases the fluorine compound is formed in good yield. When the ratio of the reagents is changed (in the case of polyalkoxy compounds) it is possible to replace not only one, but also a larger number of alkoxyl groups. Thus, for example, from diethyl diethoxytin it is possible to obtain mono- and difluorides. From tetraethoxytin with excess acetyl fluoride it is easy to form tin tetrafluoride which was first synthesized by Ruff [1] with great experimental difficulty. The reaction of acetyl fluoride with alkoxysilanes was studied with the example of tetrabutoxysilane. In this case, heating to 180° formed tributoxyfluorosilane in 60-70% yield. It should be noted that before our study, Peppard, Brown, and Johnson [2] investigated the reaction of tetraethoxysilane with benzoyl fluoride; however, they did not find an exchange of alkoxy groups for fluorine.

Polyfluorosilanes are apparently easier to obtain by the Grignard reaction from silicon tetrafluoride, as we found earlier in the synthesis of ethylsilane fluorides [3].

$$SiF_4 \xrightarrow{RMgX} RSiF_3 \xrightarrow{RMgX} R_2SiF_2$$

The reaction of acetyl fluoride with alkoxysulfur compounds was studied with dimethyl sulfate. In this case formation of methyl fluorosulfonate occurred with 60% yield when the vapors of acetyl fluoride were passed into boiling dimethyl sulfate. It follows from these results that the action of carboxylic acid fluorides on alkoxy derivatives of different elements is evidently a general method for the synthesis of the corresponding fluorine derivatives. Since the starting alkoxyl derivatives of these elements and the acid fluorides are usually easy to obtain, this method has general preparative interest.

EXPERIMENTAL

1. Obtaining diethyl ethoxytin fluoride. The vapor of acetyl fluoride (1.2 g) was passed into a solution of 5 g of diethyl ethoxytin in 30 ml of absolute ether at room temperature (mole ratio 1 : 1). The mixture grew warm and at the end of the experiment colorless crystals of difluoride precipitated. These were filtered (0.8 g) and the filtrate was evaporated. The residue was a low melting, white, crystalline mass (3.5 g) which was pressed between sheets of filter paper to the consistency of a powder which can be poured. Diethyl ethoxytin fluoride melts at 90-91°.

The substance is soluble in ether and benzene. It changes with keeping: the melting point rises and becomes unsharp (105-112°). The molecular weight determination of diethyl ethoxytin fluoride (in benzene) shows that it associates.

Found %: F 8.08, 7.60; OC_2H_5 19.17. M 453, 462. $(C_6H_{15}OFSn)_2$. Calculated %: F 7.92; OC_2H_5 18.7. M 481.4.

2. Obtaining diethyltin difluoride. 2 g of diethyl diethoxytin was dissolved in 10 ml absolute ether and the solution treated with vapors of acetyl fluoride. The precipitated crystals were filtered and washed with ether. Diethyltin difluoride was crystallized from anhydrous alcohol. Yield 1.4 g (85%).

Found %: C 22.05, 21.62; H 5.12, 4.34; F 16.55, 16.42. $C_4H_{10}F_2Sn$. Calculated %: C 22.38; H 4.65; F 17.70.

3. Obtaining tin tetrafluoride. 10 g tetraethoxytin was dissolved in 40 ml of benzene. The cooled solution was treated with acetyl fluoride (4 moles with 10% excess). After the solution was heated to boiling, the precipitate of tin tetrafluoride was filtered, washed with benzene, and dried. Yield, 4 g. The tin tetrafluoride thus obtained was an almost colorless, finely crystalline substance which deliquesces in air.

4. Obtaining tributoxyfluorosilane. 10 g (1 mole) of tetra-(n-butoxy)-silane and 2.3 g (1 mole) of acetyl fluoride were heated in a sealed tube 8 hrs at 150° and then 4 hrs at 180°, after which the product was fractionated. Tri-(n-butoxy)-fluorosilane, boiling 133-134° (32 mm) or 125-125.5° (30 mm), d^{20}_{20} 0.9383, was obtained in the amount of 3.8 g.

Found %: F 7.19, 7.30. $C_{12}H_{27}OFSi$. Calculated %: F 7.14.

5. Obtaining ethyltrifluorosilane. Silicon tetrafluoride was passed with cooling (−60°) and energetic stirring into 500 ml of absolute ether. An ether solution of 1 mole of ethylmagnesium bromide in 600 ml of ether was added to the reaction mixture through a tube which led to the bottom of the flask, and slowly, dropwise over 2 hrs, so that the temperature in the reaction mixture did not rise above −60°, after which the addition of silicon tetrafluoride was continued for another 15 min. Then the contents of the flask along with the acetic acid which had condensed in it were distilled. The fraction with boiling point to +10° was redistilled repeatedly. We obtained 45 g of ethyltrifluorosilane boiling at −4-2°. The yield was about 40% (based on magnesium).

Found %: F 49.52. M 113.4. $C_2H_5F_3Si$. Calculated %: F 49.91. M 114.1.

6. Obtaining diethyldifluorosilane. The synthesis was carried out in a manner analogous to that of Expt. 5. Saturation with gaseous SiF_4 took place at 10-15°. The introduction of 1 mole of ethylmagnesium chloride was carried out dropwise over 45-50 min. After the ether was distilled off in a column with 10 theoretical plates the residue was fractionated. We obtained 10 g of diethyldifluorosilane with boiling point 61.5-62°.

Found %: F 30.65. M 124.0 (in benzene). $C_4H_{10}F_2Si$. Calculated %: F 30.60. M 124.1.

7. Obtaining methyl fluorosulfonate. The vapors of acetyl fluoride (7 g) were bubbled into 12.5 g of freshly distilled dimethyl sulfate at the boiling point. Reaction was energetic. In the receiver, connected to a reflux condenser, we collected about 4 ml of unreacted acetyl fluoride which was returned to the reaction mixture. By repeated redistillations we obtained 3 g of methyl acetate, boiling 57-58°, 3.5 g of a mixture of methyl acetate with methyl fluorosulfonate boiling 75-80°, and 4.5 g of methyl fluorosulfonate boiling 92°, d^{20}_{20} 1.3998. 2 g of dimethyl sulfate and about 1 g of acetyl fluoride did not enter into reaction. The yield of methyl fluorosulfonate was 50-60% based on reacting dimethyl sulfate.

SUMMARY

We have studied the reaction of acetyl fluoride with alkoxy derivatives of Sn, Si and S; we have found that in this reaction there occurs replacement of alkoxy groups by fluorine with formation of the corresponding fluoroorganic compounds.

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THE TAUTOMERISM OF 9-AMINOACRIDINE

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Spectrographic study in the ultraviolet of 2- and 4-amino- [1], 2- and 4-hydroxy- [2], and 2- and 4-methylpyridine [3] has shown that tautomerism of these substances, according to absorption spectra, does not occur. The literature on the spectrum study of 9-aminoacridine [4-7, 11, 12] is contradictory. In the present paper we consider the absorption spectrum in the ultraviolet of 9-aminoacridine and 10-methyl-9-iminoacridine.

The synthesis of these substances was carried out according to the literature data [8, 9]. 9-Aminoacridine after recrystallization from acetone formed light yellow crystals with m. p. 236° (236-237° [10]). 10-Methyl-9-iminoacridine after recrystallization from absolute ether appeared as light orange needles with m. p. 134-136° (134-136° [9], 134° [7]).

We repeated in part the studies described in the literature of 9-aminoacridine in ethanol, dioxane and weak solutions of hydrochloric acid and sodium alcoholate, and also ran studies in comparatively concentrated solutions of hydrochloric, sulfuric, and nitric acids. 10-Methyl-9-iminoacridine also was studied spectroscopically in ether, hexane, and dioxane with addition of small amounts of water. In all the solvents, the studies were carried out at 10^{-3} to 10^{-5} molar concentrations. 10-Methyl-9-iminoacridine was studied in dioxane from 10^{-2} to 10^{-5} molar, and in hexane, because of the great insolubility, from 10^{-4} to 10^{-5} molar solutions.

The absorption spectrum of 9-aminoacridine in organic solvents is characterized by two very intense absorption bands which lie between λ 4400-3200 and 2800-2400 A (Fig. 1, curves 1 and 2). Comparison of the absorption spectrum of acridine in ethanol and 9-aminoacridine in ethanol and dioxane (Fig. 1, curves 1, 2, and 3) shows that they are similar, except that the absorption curve for 9-aminoacridine differs from the curve for acridine by a shift toward the visible. Under the influence of the amino group the long wave "benzene" maximum of acridine is shifted by 500 A, and the short wave maximum by 100 A; the intensities of these bands remain almost unchanged. In general, the spectrum of 9-aminoacridine in organic solvents can be considered as a complex "benzeneaminopyridine" absorption spectrum, in which the "pyridine" and "p-aminopyridine" bands are not clearly apparent. However, the "p-aminopyridine" band with a maximum oriented at about λ 2600 A is seen in the spectra of its derivatives, 2-methoxy-9-aminoacridine (Fig. 1, curve 4), and the "pyridine" band with an approximate maximum at λ 3125 A (one of the bands in the fine structure of pyridine) was detected by Acheson [7] on the curve of 9-aminoacridine in methanol.

9-Dimethylaminoacridine, studied as a standard of the tautomeric amino form [7], has in its absorption spectrum a satisfactory similarity to 9-aminoacridine (Fig. 1, curve 5) and differs from the latter only in the fine structure of the long wave "benzene" band. Such a fine structure of the "benzene" band is also found in its derivative, 2-methoxy-9-aminoacridine (Fig. 1, curve 4).

In the standard solutions of hydrochloric acid in ratios 1 : 0.1, 1 : 1, and 1 : 100 moles of HCl (Fig. 1, curves 6-8) the absorption spectrum of 9-aminoacridine shows a fine structure in its long wave "benzene" band with λ_{max} 4235, 4000, and 3800 A, and a fine structure in the "pyridine" bands with λ_{max} 3250 and 3100 A, but a "p-aminopyridine" band with a maximum about λ 2600 A, as in the neutral solutions, is not clearly seen. Evidently, it is covered by the more intense "benzene" band of 9-aminoacridine with the same maximum at about λ 2600 A.

The fine structures of the "benzene" and "pyridine" bands seen in the absorption spectra of acid solutions of 9-aminoacridine when the concentration of hydrochloric acid changes in wide limits from 0.1 to 5 M (Fig. 1, curves 7-9, cf. curve 11) indicate that 9-aminoacridine forms a salt [4] like 4-aminoacridine [1] with just 1 equiv. of acid.

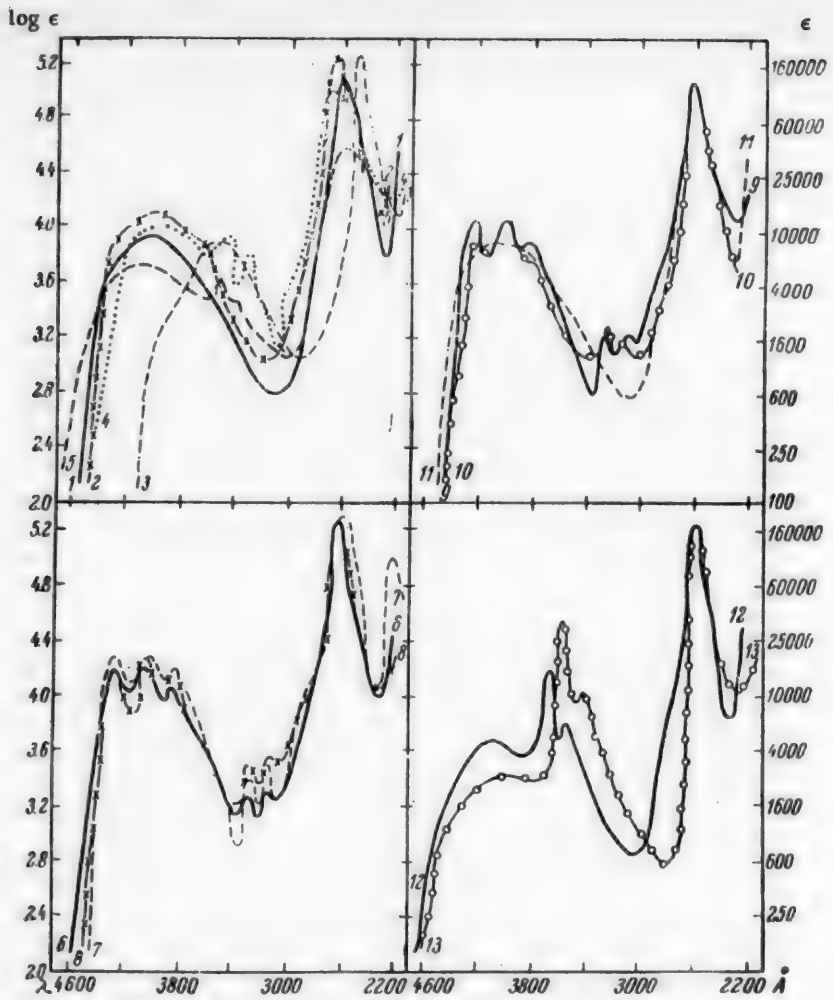


Fig. 1. Absorption spectra. 1) 9-Aminoacridine in ethanol, 2) 9-aminoacridine in dioxane, 3) acridine in ethanol, 4) 2-methoxy-9-aminoacridine in ether, 5) 9-dimethylaminoacridine in methanol [7], 6) 9-aminoacridine in ethanol solution of HCl (1 : 0.1), 7) 9-aminoacridine in ethanol solution of HCl (1 : 1), 8) 9-aminoacridine in ethanol solution of HCl (1 : 100), 9) 9-aminoacridine in 5 molar ethanol solution of HCl, 10) 9-aminoacridine in 20% H_2SO_4 (after dilution of a water solution in 17.5 M H_2SO_4), 11) 9-aminoacridine in ethanol, 12) 9-aminoacridine in concentrated (17.5 M) H_2SO_4, 13) acridine in 17.5 M H_2SO_4.

The absorption spectrum of 9-aminoacridine in concentrated sulfuric acid approximates to the structure of unsubstituted acridine (Fig. 1, curves 12 and 13), in the same acid. This can be explained, in spite of the literature data [13], by the formation of a salt also on the amino group. In order to determine whether sulfonation of 9-aminoacridine by concentrated sulfuric acid occurs, we diluted the solution to 20% sulfuric acid. The absorption spectrum in 20% sulfuric acid (Fig. 1, curve 10) agreed with the curve for absorption in the standard 5 M solution of hydrochloric acid (Fig. 1, curve 9). This confirms that in concentrated sulfuric acid there is only salt formation.

A study of the absorption spectrum of 10-methyl-9-iminoacridine in anhydrous hexane, ether, and dioxane (Fig. 2, curves 1-3) showed that it had nothing in common with the spectra of 9-aminoacridine and 9-dimethyl-

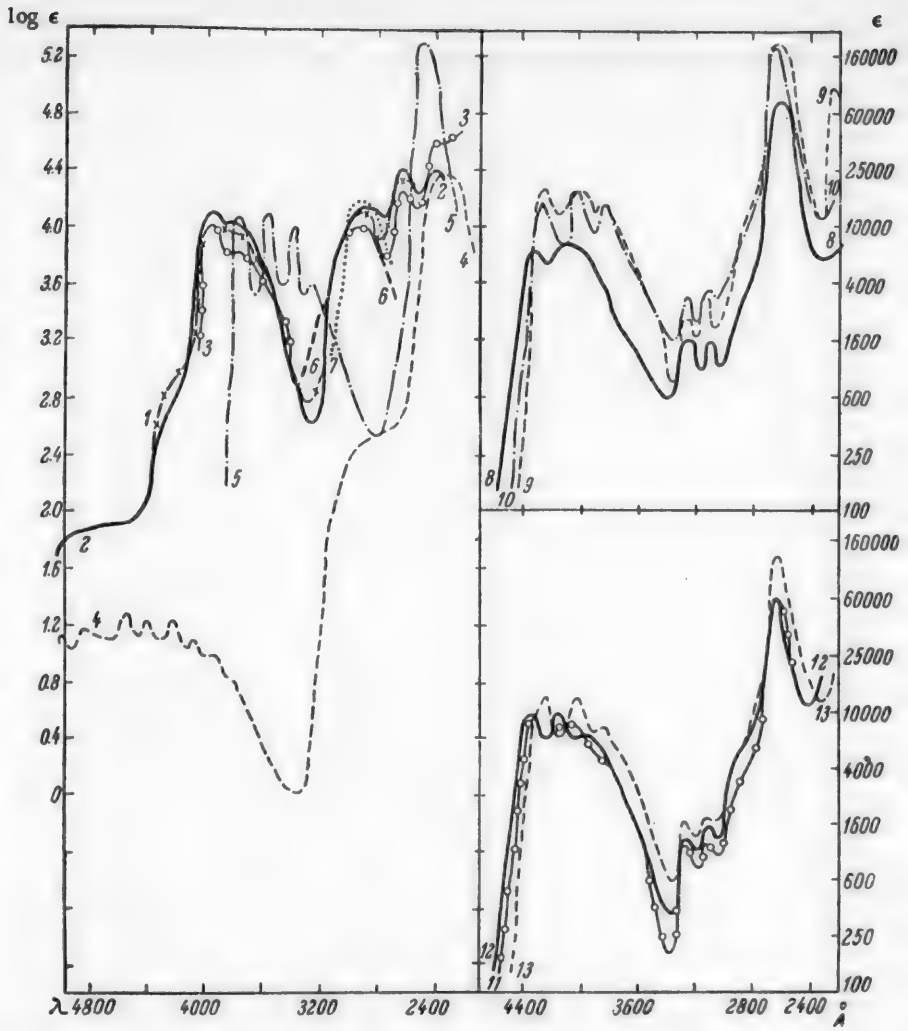


Fig. 2. Absorption spectra. 1) 10-Methyl-9-iminoacridine in ether, 2) 10-methyl-9-iminoacridine in dioxane, 3) 10-methyl-9-iminoacridine in hexane, 4) p-benzoquinone [14] in hexane, 5) anthracene in hexane, 6) dihydroacridine in ethanol [15], 7) diphenyl amine in ethanol [16], 8) 10-methyl-9-iminoacridine in water, 9) 9-aminoacridine in alcohol solution of HCl (1:1), 10) 9-aminoacridine hydrochloride in ethanol, 11) 10-methyl-9-iminoacridine in ethanol solution of HCl (1:100), 12) 10-methyl-9-iminoacridine in 5 M ethanol solution of HCl, 13) 9-aminoacridine in 5 M ethanol solution of HCl.

aminoacridine in the same solvents. Comparison of the absorption spectrum of 10-methyl-9-iminoacridine and p-benzoquinone [14] (Fig. 2, curves 1 and 4) in hexane showed their similarity. The absorption maxima of the three bands occurred almost at the same wavelength and only two of them differed in intensity. It is interesting that one of the three absorption bands at a maximum of λ 2900 A and ε 12,000 is also characteristic for dihydroacridine [15] and diphenyl amine [16]. When we compare the absorption spectrum of 10-methyl-9-iminoacridine with the absorption spectrum of anthracene (Fig. 2, curves 1 and 5) we can see that the bands with maxima at λ 3950 A and ε 12,000, λ 3800 A, ε 9000, and λ 2650 A, ε 20,000 are "benzene" bands. Hence the absorption spectrum of 10-methyl-9-iminoacridine must be regarded as complex: "benzene" bands are superimposed on the "quinone" spectrum.

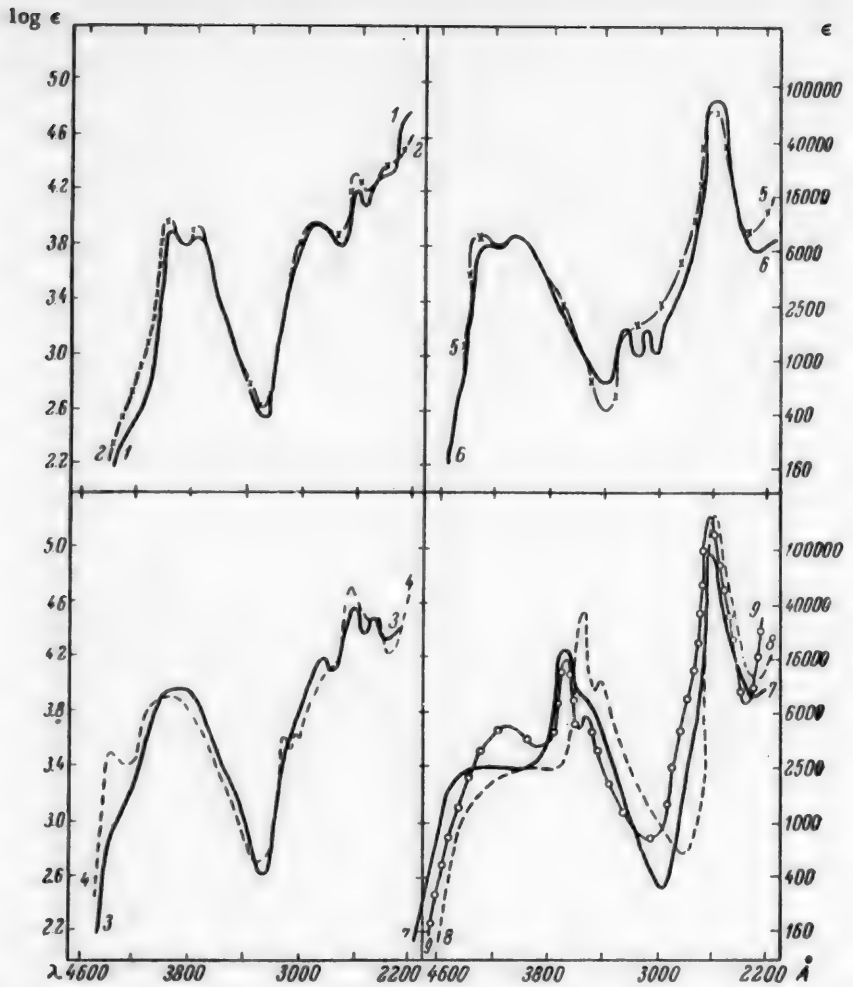
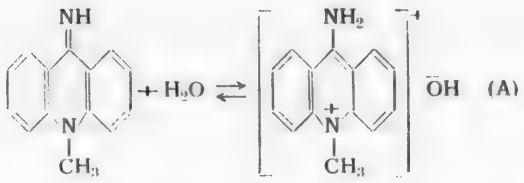


Fig. 3. Absorption spectra. 1) 10-Methyl-9-iminoacridine in dioxane–water solution (0.1% water), 2) 10-methyl-9-iminoacridine in dioxane–water solution (2% water), 3) 10-methyl-9-iminoacridine in dioxane–water solution (10% water), 4) 10-methyl-9-iminoacridine in dioxane–water solution (water 20%), 5) 10-methyl-9-iminoacridine in dioxane–water solution (50% water), 6) 10-methyl-9-iminoacridine in water, 7) 10-methyl-9-iminoacridine in 17.5 M H_2SO_4, 8) acridine in 17.5 M H_2SO_4, 9) 9-aminoacridine in 17.5 M H_2SO_4.

Under the influence of such polar solvents as water and also in acid solutions there is a strong change in the absorption spectrum of 10-methyl-9-iminoacridine; its character is like that of 9-aminoacridine in ethanolic hydrochloric acid (Fig. 2, curves 8-12). This similarity occurs because of salt formation both for 10-methyl-9-iminoacridine and for 9-aminoacridine which form acridine ions with the same structure.

The absence of "quinone" bands in the spectrum of 9-aminoacridine dissolved in organic solvents or in acids, and the actually observed "pyridine" bands in its absorption spectrum confirm the correctness of the conclusion concerning the amine structure of 9-aminoacridine.

Considering that in water solution the absorption spectrum of 10-methyl-9-iminoacridine is identical with that of 9-aminoacridine in acids, we tried to prepare equilibrium mixtures of the two tautomeric forms by dissolving 10-methyl-9-iminoacridine in dioxane–water solutions with different quantities of water in the dioxane. When we added between 0.1 and 2% water to dioxane, no change was seen in the "benzene-quinone" spectrum of 10-methyl-9-iminoacridine (Fig. 3, curves 1 and 2). Equilibrium was shifted to the side of the amino form at contents of 2 to 30% water in the dioxane (scheme A). A change in the absorption spectrum then occurred (Fig. 3, curves 3 and 4). A similar equilibrium reaction with water in dioxane has previously been observed for N-methyl-α-pyridoneimine [18, 19].



With 40-50% water in the dioxane, the "quinone" bands of 10-methyl-9-iminoacridine were not observed (Fig. 3, curves 5 and 6) which indicates the practically complete transformation of the imino to the amino form.

The absorption curve of 10-methyl-9-iminoacridine dissolved in dioxane–water solutions was compared with the absorption curve of 9-aminoacridine obtained under conditions of catalytic action on it of ethanol solutions of small amounts of acid and alkali; comparison was made immediately after preparing the solutions of 9-aminoacridine, and two days later. In all cases only the "benzene-aminopyridine" bands were observed in the 9-aminoacridine spectrum, characterizing the amino form, and no similarity was seen with the curves of 10-methyl-9-iminoacridine which would have shown an equilibrium of both forms of the assumed tautomers.

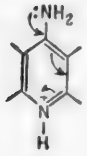
The absorption spectrum of 10-methyl-9-iminoacridine in concentrated sulfuric acid hardly differs from that of 9-aminoacridine in the same acid (Fig. 3, curves 7 and 9). Such a resemblance in spectra indicates the formation in 10-methyl-9-iminoacridine of a doubly charged cation like that of 9-aminoacridine.

DISCUSSION OF RESULTS

The introduction of an amino group in the acridine ring in position 9 causes a marked shift in the "benzene" bands toward the visible, but without notable increase in their intensity compared to acridine, while the "pyridine" bands are not shifted, but their intensity is decreased in nonionizing solvents by about 6 times, and in ionizing solvents by about 3 times. This may be because when the benzene and aminopyridine rings are condensed in 9-aminoacridine they interact, as in 4-aminoquinoline [17]. Two types of interaction are seen: 1) interaction of the condensed benzene and pyridine rings; "benzene" and "pyridine" bands are seen in the spectrum; 2) interaction of the amino group with the ring and the ring nitrogen. The weak participation of the amino group in union with the π-electrons of the pyridine ring in the study of 9-aminoacridine in nonionizing solvents can be explained by association of the molecules [13, 20, 21].

The effect of such ionizing solvents as an ethanol solution of hydrogen chloride even at ratios of 9-aminoacridine and HCl of 1 : 0.1 (9-aminoacridine is insoluble in water) causes separation of the associated molecules and the formation of 9-aminoacridine ions in whose spectra the "pyridine" bands with fine structure are clearly visible.

In the ion there is a redistribution of electron density from the amino group to the positively charged nitrogen (scheme B). A combination occurs between the amino groups, the π-electrons of the pyridine ring, and the electron-attracting ring nitrogen which is similar to that found in 4-aminopyridine or 4-aminoquinoline [1, 17].



(B)

Simultaneously with the appearance in the spectra of ethanol solutions of 9-aminoacridine of "pyridine" bands with fine structure, there should occur "p-aminopyridine" bands corresponding to the combination of groups. However, such "p-aminopyridine" bands with maxima at about λ 2600 A were not observed only because they were covered by the more intense short wave "benzene" bands with maxima at the same wavelength.

Profiting by the fact that when OH, OCH_3 or NH_2 groups are introduced into the benzene ring of 9-aminoacridine the "benzene" bands undergo a bathychromic shift, we succeeded in showing clearly in 2-methoxy-9-aminoacridine that "p-aminopyridine" band absorption was present.

When salts of 9-aminoacridine are formed, its "benzene aminopyridine" absorption spectrum is almost unchanged, which indicates that 9-aminoacridine is a tautomeric compound. Actually, in an ethanol solution of hydrochloric acid the absorption spectrum of 10-methyl-9-iminoacridine is identical with the spectrum of salts of 9-aminoacridine formed on the ring nitrogen.

This similarity of the spectra of 9-aminoacridine and 10-methyl-9-iminoacridine in acids even with their different structures can be explained by the fact that in the first, the salt-forming center is the ring nitrogen and in the second, the nitrogen of the imino group. As a result, salt formation in each case will give an ion of 9-aminoacridine with the same structure, which explains the identity of their absorption spectra in acid media.

These data do not solve the question of where the proton of 9-aminoacridine is actually found: on the ring nitrogen, or on the amino group. The answer will be obtained by investigation of 10-methyl-9-iminoacridine in anhydrous dioxane, hexane, or absolute ether.

In the spectrum of 10-methyl-9-iminoacridine in anhdrous dioxane, for example, there are bands which correspond to quinone or quinone imine. Close similarity also exists with dihydroacridine or diphenyl amine with band maximum at λ 2900 A.

In the spectrum of 9-aminoacridine in the same solvents we observed "pyridine" bands and did not find "quinone imine" or "diphenylamine" absorption bands. On the basis of this difference we assumed an amine structure for 9-aminoacridine and so we should reject the hypothetical tautomeric imino form.

The data of our spectrographic study of the amine structure of 9-aminoacridine agree with the measurements of dipole moment. The observed dipole moment of 9-aminoacridine is 4.13 D [22], which considerably exceeds the dipole moment calculated on its amino group, 3.28 D. The excess of the dipole moment of 0.85 D above the calculated value confirms the correctness of our spectrographic data, that between the ring nitrogen, the π-electrons of the pyridine ring, and the amino group of 9-aminoacridine there is a combination. In the absence of such a combination of the amino group with the ring nitrogen through the π-electron system of the pyridine ring, the dipole moment calculated on the imino form of 9-aminoacridine should be 1.65 D, which does not agree with the experimental value.

The double reactive ability of 9-aminoacridine can be explained in accord with the views of A. N. Nesmeianov [23, 24] by the course of reaction with a transferred reaction center.

SUMMARY

1. We have studied the effect of solvents and acids on the absorption spectrum of 9-aminoacridine and 10-methyl-9-iminoacridine.

2. We have shown that the "benzene-aminopyridine" absorption spectrum of 9-aminoacridine is almost unchanged when salts are formed on the ring nitrogen.

3. Salt formation by 9-aminoacridine in concentrated sulfuric acid is characterized by the formation of a doubly charged 9-aminoacridine cation.

4. We have shown that the absorption spectra of 9-aminoacridine and 10-methyl-9-iminoacridine in anhydrous dioxane are different, but are similar in solutions of hydrogen chloride and concentrated sulfuric acid.

5. We have shown that 9-aminoacridine in ethanol solutions of hydrochloric acid forms salts by binding the proton on the ring nitrogen, and in 10-methyl-9-iminoacridine, on the nitrogen outside the ring.

6. We have established the absence of tautomerism in 9-aminoacridine by the ultraviolet absorption spectrum.

In conclusion, I express deep thanks to V. I. Blizniukov, under whose direction this investigation has been carried out.

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THE SYNTHESIS OF 5,6,7-TRIMETHYLISOALLOXAZINES

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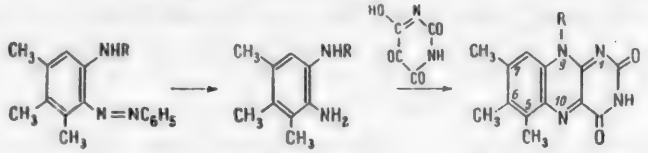
We have earlier shown [1] that a methyl group in the ortho-position to the azo group in 3,4,5-trimethylphenyl-2-phenylazo-1-D-glucamines, which are starting substances for the synthesis of isoalloxazines, causes stereochemical difficulties in reaction and a strong shift in ultraviolet absorption bands. It was interesting to trace this effect on the spectral characteristics of isoalloxazine compounds themselves when a methyl group was in positions 5, 6, and 7, reflecting the structure of riboflavin (positions 6 and 7) and also the structure of one of the stronger antivitamins, isoriboflavin [2] (positions 5 and 6). Since the spacial isomerism of the pentose side chain of 3,4-dimethylphenyl-1-D-glucamine affects its reactivity [3], we also tested the effect of such isomerism in 3,4,5-trimethylphenyl-2-amino-1-D-glucamines (I-IV). For a solution of these problems we prepared 5,6,7-trimethylisoalloxazines (V-VIII) with tetrahydroxyalkyl substituents in position 9 which corresponded to the configurations of the hydroxy groups of all four possible pentose groups: D-ribose, D-arabinose, D-xylose, and D-lyxose. The corresponding 3,4,5-trimethyl-2-phenylazo-1-D-glucamines were transformed by catalytic hydrogenation into 3,4,5-trimethyl-o-phenylenediamino compounds (I-IV) which were condensed with alloxane into isoalloxazines (V-VIII); condensation was carried out at 50° in the presence of boric acid as a catalyst.



(I),(II),(III),(IV) (V),(VI),(VII),(VIII)

R = pentose residues: d-ribose (I and V), d-arabinose (II and VI), d-xylose (III and VII), and d-lyxose (IV and VIII).

Isoriboflavin [4] was obtained from 3,4-dimethylphenyl-2-phenylazo-1-D-ribose amine which was reduced to 3,4-dimethylphenyl-2-amino-1-D-ribose amine; this diamine was condensed with alloxane.

The absorption spectra of riboflavin, isoriboflavin, and the new 5,6,7-trimethylisoalloxazines (V-VIII) are characterized by the data given in Table 1 and shown in Fig. 1.

TABLE 1

Substance	Position of CH_3 groups	Relative ultraviolet fluorescence	Absorption maximum 1		2		3		4	
			λ mμ	ε · 10^4	λ mμ	ε · 10^4	λ mμ	ε · 10^4	λ mμ	ε · 10^4
Riboflavin	6 & 7	100	223	2.86	268	3.15	372	1.06	445	1.19
Isoriboflavin	5 & 6	21	—	—	268	3.38	382	1.06	448	0.67
Trimethylisoalloxazine derivatives (V-VIII)	5,6 & 7	20—23	223	2.27	268	3.21	394	1.44	446	0.88

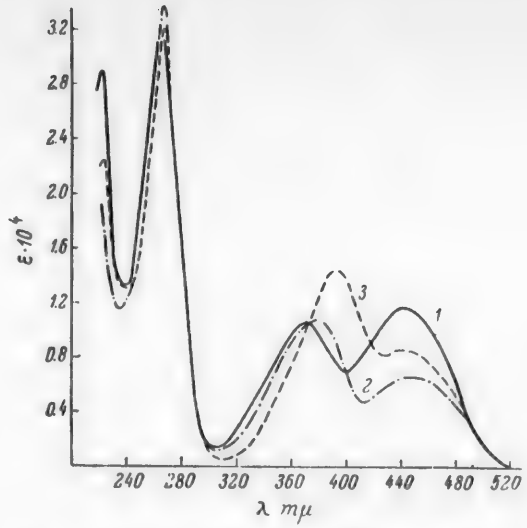


Fig. 1. Ultraviolet absorption spectra (in water). 1) 6,7-Dimethyl-9-(1'-D-ribityl)-isoalloxazine (riboflavin); 2) 5,6-dimethyl-9-(1'-D-ribityl)-isoalloxazine (isoriboflavin); 3) 5,6,7-trimethyl-9-(1'-D-ribityl)-isoalloxazine.

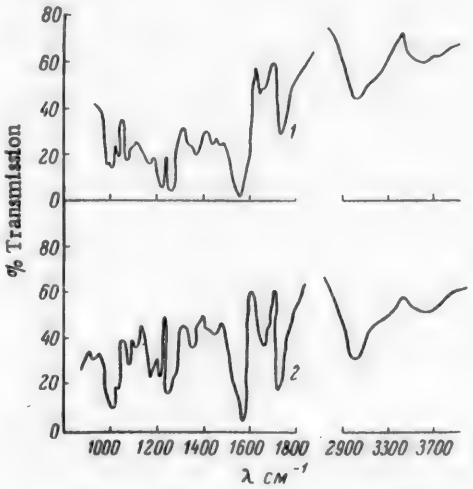


Fig. 3. Infrared absorption spectra (in CCl_4). 1) 5,6,7-Trimethyl-9-(1'-D-ribityl)-isoalloxazine; 2) 6,7-dimethyl-9-(1'-D-ribityl)-isoalloxazine (riboflavin) (d = 500 μ).

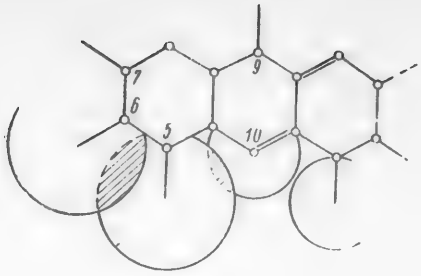


Fig. 2.

The introduction of a methyl group in the position "peri" to the hetero-nitrogen atom causes a strong decrease in intensity of absorption up to 60-70% in the visible. There then occurs a shift in the 3rd ultraviolet maximum of 10 mμ for isoalloxazines with methyl groups in positions 5 and 6, and of 22 mμ for derivatives with methyl groups in positions 5, 6, and 7 of the isoalloxazine ring.

No effect of configuration of hydroxyls of the pentoses substituted in the 3,4,5-trimethylphenyl-2-amino-D-glycamines was observed in the condensations with alloxane.

The shift in ultraviolet absorption maxima and the decreased intensity of absorption in the visible part of the spectrum for isoalloxazines with a large substituent in the position "peri" to the hetero-nitrogen must be regarded as involving spatial difficulties, forcing this nitrogen atom out of the plane of the ring and at the same time breaking the coplanar structure of the system of conjugated double bonds $-N=C-\overset{|}{C}=N-$ into which enters the azomethine chromophoric group $-N=C<$ (cf. Fig. 2).

Flavins have a typical ability to fluoresce, and some of them glow intensely in ultraviolet light. It is known that introduction of a methyl group in the position "peri" to the hetero-nitrogen atom (position 5) causes a sharp decrease in intensity of fluorescence; this confirms the idea that just the system of conjugated double bonds, coplanar with the plane of the molecule, gives the flavin its power to fluoresce.

For 5,6-dimethyl-9-(1-D-ribityl)-isoalloxazine (riboflavin) and 5,6,7-trimethyl-9-(1-D-ribityl)-isoalloxazine (V), using the method of infrared absorption, we obtained the oscillation spectra at frequencies 800-1800 cm^{-1} and 2700-4000 cm^{-1} (Fig. 3). The introduction of an additional methyl groups in the isoalloxazine ring does not make much change in the spectra and in the characteristic frequencies of the groups C=C, C=N, and C=O. The absorption maxima in the oscillation frequencies of OH, CH, and NH are the same in these two spectra, and the absorption curves of the latter groups overlap and cannot be fully resolved.

The infrared absorption spectra were taken by L. V. Luk'ianova to whom the authors express their thanks.

EXPERIMENTAL

Aminoglucamines. 3 g of 3,4,5-trimethylphenyl-2-phenylazo-1-D-glucamine or 3,4-dimethylphenyl-2-phenylazo-1-D-ribitylamine in 60 ml of alcohol were hydrogenated with 3 g of skeleton nickel catalyst at 85-100° in a rotating autoclave at 60 atmos pressure for 3 hrs. Then, after removing the catalyst, the aminoglucamines were isolated from the colorless alcohol solution in the form of colorless needles; these were recrystallized from alcohol. The resulting 3,4,5-trimethylphenyl-2-amino-1-D-glucamines (I-IV) are described in Table 2.

TABLE 2

Substance	Substituent R	Melting point	Yield (in %)	Analysis (% N) found	Analysis (% N) calc. for $C_{14}H_{24}O_4N_2$
(I)	D-Ribityl	137—138°	58	9.60, 9.66	9.85
(II)	D-Arabityl	141—143	77	9.81, 9.94	9.85
(III)	D-Xylityl	137—138	71	10.19, 10.13	9.85
(IV)	D-Lyxityl	(Used without isolation from the solution)			

3,4,-Dimethylphenyl-2-amino-1-D-ribitylamine was obtained as colorless needles, melting at 138-140°, yield 37%.

Found %: N 10.06, 9.93. $C_{13}H_{22}O_4N_2$. Calculated %: N 10.36.

Isoalloxazines. To a solution of 2 g alloxane in 30 ml boiling glacial acetic acid was added a boiling solution of 4 g of boric acid in 30 ml of glacial acetic acid. The partly crystallized boric-alloxane complex was treated at 50° with 2 g of aminoglucamine in 30 ml of glacial acetic acid and the mixture was kept for 1 hr at 50°. Then the solvent was distilled off in a vacuum, the dry residue was washed with 10-15 ml of water and the flavin was reprecipitated from 8-10 ml of concentrated hydrochloric acid by 15-fold dilution with water. The resulting 5,6,7-trimethylisoalloxazines (V-VIII) are described in Table 3.

TABLE 3

Substance	Substituent R	Melting point	Yield (in %)	Analysis (%N) found	Analysis (%N) calc. for $C_{18}H_{22}O_6N_4$
(V)	D-Ribityl	269° (decomp.)	50	14.03, 13.89	14.35
(VI)	D-Arabityl	279 (decomp.)	75	14.32, 14.20	14.35
(VII)	D-Xylityl	282 (decomp.)	51	14.24, 14.46	14.35
(VIII)	D-Lyxityl	278 (decomp.)	33	13.90, 13.85	14.35

Isoriboflavin, 5,6-dimethyl-9-(1-D-ribityl)-isoalloxazine was obtained from 3,4-dimethylphenyl-2-amino-1-D-ribitylamine in the form of yellow needles melting at 264° (decomposition) with a yield of 70%.

Found %: N 14.87, 14.84. $C_{17}H_{20}O_6N_4$. Calculated %: N 14.88.

SUMMARY

1. We have shown that the fluorescence of isoalloxazines is due to the conjugated system $-N=C-\underset{|}{C}=N-$ and its intensity depends on the coplanarity of this system with the plane of the molecule.

2. We have obtained 8 new compounds of which 4 are new flavins.

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ESTERS OF AMINOPHENYLSULFONAMIDOPHOSPHORIC ACID

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Dimethyl and diphenyl esters of o-, m- and p-aminophenylsulfonamidophosphoric acid (N^1-phosphates of aminobenzenesulfonamide) were obtained according to the scheme

$$NO_2C_6H_4SO_2NH_2 \xrightarrow{PCl_5} NO_2C_6H_4SO_2N{=}PCl_3 \xrightarrow{HCOOH}$$
$$\rightarrow NO_2C_6H_4SO_2NHPOCl_2\,[1] \xrightarrow{2NaOR} NO_2C_6H_4SO_2NHPO(OR)_2\,[2] \xrightarrow{6H}$$
$$\rightarrow NH_2C_6H_4SO_2NHPO(OR)_2.$$

Reduction of the diesters of nitrophenylsulfonamidophosphoric acid was carried out with molecular hydrogen in the presence of a platinum catalyst in alcohol solution at room temperature and a pressure of about 100 mm Hg. The yields were quantitative.

The dimethyl and diphenyl esters of aminophenylsulfonamidophosphoric acids (I) were colorless crystalline substances with weak basic and strongly acid properties. They dissolved easily in aqueous soda solutions, titrated as monobasic acids, and their water solutions were acid to Congo paper.

The dimethyl esters of aminophenylsulfonamidophosphoric acids were easily soluble in hot water and were diazotized under ordinary conditions (like aniline). The diphenyl esters dissolved in hot water with difficulty, but easily in alcohol, and were diazotized under the same conditions as aromatic amines with electronegative substituents (for example, nitroaniline).

TABLE 1

Esters of Aminophenylsulfonamidophosphoric Acid $NH_2C_6H_4SO_2NHPO(OR)_2$ (I)

Substance no.	Position of amino group in benzene	R	From what crystallized, crystal form	Melting point	Found			Empirical formula	Calculated*	
					N (%)	OCH_3 (%)	equiv.		N (%)	OCH_3 (%)
(III)	ortho	CH_3	Alcohol, prisms	124—127°	10.27	21.8	1.002	$C_8H_{13}O_5N_2SP$	10.00	22.14
(IV)	meta	CH_3	Water, prisms	192—194	10.28	22.17	1.015	$C_8H_{13}O_5N_2SP$	10.00	22.14
(V)	para	CH_3	Alcohol, needles	146—148	9.9	21.63 22.15	1.007	$C_8H_{13}O_5N_2SP$	10.00	22.14
(VI)	ortho	C_6H_5	Alcohol, needles	166—168	7.14	—	0.980	$C_{18}H_{17}O_5N_2SP$	6.93	—
(VII)	meta	C_6H_5	50% Alcohol, prisms	232—234	7.16	—	0.978	$C_{18}H_{17}O_5N_2SP$	6.93	—
(VIII)	para	C_6H_5	Alcohol, prisms	225—226	6.98	—	1.004	$C_{18}H_{17}O_5N_2SP$	6.93	—

* Calculated equiv.: 1.0.

TABLE 2

Esters of Benzoylaminophenylsulfonamidophosphoric Acids $C_6H_5CONHC_6H_4SO_2NHPO(OR)_2$ (II)

Substance no.	Position of amino group in benzene ring	R	From what crystallized, form of crystals	Yield (in %)	Melting point	Found			Empirical formula	Calculated*	
						N (%)	OCH_3 (%)	equiv.		N (%)	OCH_3 (%)
(IX)	ortho	CH_3	Benzene, needles	71.0	151—152[c]	7.34	15.56, 15.78	0.993	$C_{15}H_{17}O_6N_2SP$	7.29	16.14
(X)	meta	CH_3	Alcohol, needles	73.0	171—173	7.31	15.46, 16.00	0.985	$C_{15}H_{17}O_6N_2SP$	7.29	16.14
(XI)	para	CH_3	Alcohol, needles	81.0	222—224	7.16	16.07, 15.98	1.003	$C_{15}H_{17}O_6N_2SP$	7.29	16.14
(XII)	ortho	C_6H_5	Water, needles	80.0	142—144	5.51	—	1.007	$C_{25}H_{21}O_6N_2SP$	5.51	—
(XIII)	meta	C_6H_5	Alcohol, needles	79.0	206—208	5.65	—	1.002	$C_{25}H_{21}O_6N_2SP$	5.51	—
(XIV)	para	C_6H_5	Alcohol, prisms	86.2	219—221	5.52	—	1.010	$C_{25}H_{21}O_6N_2SP$	5.51	—

• Calculated equiv.: 1.0.

It is known that amides of o-, m-, and p-aminobenzenesulfonic acids (of which substances(I)are a derivative) melt closely together (153, 142, and 163°, respectively); the meta-isomer is the lowest melting, the para-isomer the highest [3]. In the case of(I)the differences in melting points of ortho-, meta-, and para-isomers is very considerable (see Table 1) and the meta-isomer is the highest melting, the ortho-isomer the lowest. Ortho-isomers of (I) are very easily soluble in acetone at room temperature, the para-isomers dissolve with difficulty on heating, and the meta-isomers are practically insoluble in acetone. Probably the changed melting points and great differences in acetone solubility are explained by the formation of intra- and intermolecular hydrogen bonds for ortho- and para-isomers, respectively, while these are formed with difficulty or not at all for the meta-isomers. The effect of hydrogen bonds on the melting points of aminobenzenesulfonamides is very much less because of the absence of polarizing effect of the phosphoric acid residue, and so they melt more closely together.

We characterized substances (I) by obtaining their benzoyl derivatives by the Schotten-Bauman reaction. They are colorless, crystalline substances with strong acid properties and no basic properties. Their water solutions have an acid reaction to Congo paper. Their melting points in some cases are higher and in some cases lower than the melting points of the corresponding (I) substances. For the other properties of substances (I) and (II), see the experimental part and Tables 1 and 2.

EXPERIMENTAL

General method of obtaining esters of aminophenylsulfonamidophosphoric acid (I). 0.01 mole of the corresponding diester of nitrophenylsulfonamidophosphoric acid [2] was dissolved with heat in 50.0 ml of 96% alcohol and the solution was quickly cooled with energetic stirring so that the nitrocompound crystallized in the smallest possible crystals. We added 0.1 g of platinum oxide [4] and carried out the reduction with hydrogen at a pressure of about 100 mm Hg with continuous shaking. Reduction at first went rapidly accompanied by strong heating and therefore the reaction mixture had to be cooled with ice. During the reduction the nitrocompound gradually dissolved. In some cases near the end of the reaction, substance (I) began to crystallize out. After 1-2 hrs, the theoretical amount of hydrogen had been absorbed and reduction stopped. In the case of substances (III, V, VI) at the end of the reduction the platinum was filtered off, and the alcohol was evaporated in a vacuum on the water bath; the residue was recrystallized from alcohol. In the case of substances(IV),(VII), and (VIII) the reaction products

were filtered along with the platinum and then recrystallized: (IV) from boiling water, (VII) from 50% alcohol, and (VIII) from 96% alcohol (1.0 g per 250 ml alcohol). Yields were quantitative. All substances (I) were insoluble in benzene, CCl_4, petroleum ether, and ether. For the solubility in acetone, see above.

Esters of benzoylaminophenylsulfonamidophosphoric acid (II). A mixture of 0.002 g-molecules of the corresponding (I), 2.0 ml of 1 N sodium hydroxide solution, 2.0 ml of 2 N soda solution, and 0.003 g-molecules of benzoyl chloride were energetically shaken until the odor of benzoyl chloride vanished (30-40 min). Then the solution was acidified with 2 N hydrochloric acid. (XI) and (XIV) precipitated directly in the crystalline state, and the other substances (II) came down as thick oils which quickly crystallized completely. To remove the benzoic acid, (IX) was washed with ether (3 × 3.0 ml) and all the other substances (II) were washed with boiling water (4 × 3.0 ml). In boiling water (IX) was easily soluble, (X-XII) were soluble with difficulty, (XIII) with great difficulty, and (XIV) was insoluble. In cold alcohol (IX) and (XII) dissolved easily, (X), (XIII) and (XIV) dissolved in boiling alcohol, and (XI) was difficultly soluble in boiling alcohol. (X), (XI), (XIII), and (XIV) were insoluble in benzene, CCl_4 and ether; (XII) was easily soluble in cold benzene, and (IX) in boiling benzene. (XII) was easily soluble in boiling CCl_4, (IX) dissolved with difficulty. (XII) dissolved easily in cold ether, (IX) was insoluble. None of substances (II) dissolved in petroleum ether. (IX) and (XII) dissolved easily at room temperature in acetone, (XIII) and (XIV) dissolved with somewhat more difficulty, and (X) and (XI) were little soluble in boiling acetone. Thus the ortho derivatives of substances (II) were the most soluble in the majority of organic solvents, and also were the lowest melting; after them came the meta-isomers, and then the para-isomers. Evidently, the effect of intramolecular hydrogen bonds in the ortho-isomers of substances II is the same as in substances (I), but the effect of intermolecular bonds in the para-isomers is almost nonexistent, probably because of blocking of the hydrogen atoms on N^4 by the benzoyl group (compare with melting points and solubilities of substances (I)).

SUMMARY

We have obtained dimethyl and diphenyl esters of aminophenylsulfonamidophosphoric acids and the corresponding benzoylaminophenylsulfonamidophosphoric acids.

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TRIARYLOXYPHOSPHAZOSULFONALKYLS AND AROMATIC ESTERS OF ALKYL SULFONAMIDOPHOSPHORIC ACIDS

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Triaryloxyphosphazosulfonalkyls were obtained by the action of sodium arylates with trichlorophosphazosulfonalkyls [1] in a benzene medium according to the scheme

$$RSO_2N{=}PCl_3 + 3ArONa$$

Sodium phenolate and sodium p-chlorophenolate react very energetically with trichlorophosphazosulfonalkyls. The reaction with dry sodium phenolate in the absence of a solvent is very violent and the reaction mixture carbonizes. In the presence of solvent reaction is quiet. Sodium p-nitrophenolate reacts less energetically; reaction proceeds when the mixture is heated on the water bath for 2-3 hrs. In Table 1 we give the yields, melting points, and analytical data for the resulting triaryloxyphosphazosulfonalkyls.

Substances I are all colorless crystals except II, without odor or taste, except for VI which has an intensely bitter taste. When the reaction mixtures are treated with water, all substances I except II precipitate as light, colorless, rectangular plates. They are all easily soluble in acetone, dioxane, and with somewhat greater difficulty in benzene (especially VI), ether and alcohol. They are soluble in boiling carbon tetrachloride and petroleum ether, insoluble in cold water, and only slightly soluble in boiling water. In their physical and chemical properties substances I are very similar to the triaryloxyphosazosulfonaryls [2], but differ somewhat in their greater solubility in boiling water and polar solvents. They are neutral, stable to water and moist air, except for VI which is very easily hydrolyzed. Even when it is dissolved in 96% alcohol it is completely saponified with formation of the p-dinitrodiphenyl ester of ethylsulfonamidophosphoric acid (IX) and nitrophenol according to the scheme

$$C_2H_5SO_2N{=}P(OC_6H_4NO_2\text{-}p)_3 + H_2O \rightarrow \underset{(IX)}{C_2H_5SO_2NHPO(OC_6H_4NO_2\text{-}p)_2} + p\text{-}NO_2C_6H_4OH.$$

In an alcohol-alkali medium, especially with heat, hydrolysis of VI goes more deeply to form a mixture of products of which IX can be isolated with a yield of not more than 50%. All the other substances I are unchanged when heated with alcohol, but are easily saponified when treated with sodium hydroxide in aqueous alcohol to form salts of the corresponding diaryl esters of alkylsulfonamidophosphoric acid (cf. [2]). With mineral acids the latter give the free diaryl esters of alkylsulfonamidophosphoric acids (VII). In Table 2 we give the yields, melting points, and analytical data for the resulting substances VII. They are colorless, crystalline substances which have a very bitter taste. They are all easily soluble in acetone and hot alcohol, very difficultly soluble in cold water and easily in hot, and difficultly soluble in most nonpolar solvents. Chemically they are strong monobasic acids. The substances VII are considerably more stable to hydrolysis by both acids and alkalis than substances I.

The structure of substances VII is clear not only because they result from saponification of substances I, but also from their synthesis by the reaction of alkylsulfonamidophosphoric acid dichlorides [3] with sodium arylates by the scheme

$$RSO_2NHPOCl_2 + 2ArONa \rightarrow RSO_2NHPO(OAr)_2 + 2NaCl$$

TABLE 1

Triaryloxyphosphazosulfonalkyls of the Type $RSO_2N{=}P(OAr)_3$ (I)

Substance no.	R	Ar	From what crystallized, form of crystals	Yield (in %)	Melting point	Found (%N)	Empirical formula	Calculated (%N)
—	CH_3	C_6H_5	Benzene, needles; ether, cubes	86.2	90—92°	3.48	$C_{19}H_{18}O_5NSP$	3.47
—	C_2H_5	C_6H_5	Benzene, prisms	83.9	100—101	3.37	$C_{20}H_{20}O_5NSP$	3.35
—	iso-C_3H_7	C_6H_5	Petroleum ether, needles	81.2	66—68	3.23	$C_{21}H_{22}O_5NSP$	3.25
(II)	n-C_4H_9	C_6H_5	Liquid $d_4^{20} \sim 1.2$	85.4	—	2.95	$C_{22}H_{24}O_5NSP$	3.14
(III)	$C_6H_5CH_2$	C_6H_5	Benzene, prisms; water, rectangular plates	86.5	89—90	2.86	$C_{25}H_{22}O_5NSPCl_3$	2.92
(IV)	C_2H_5	p-ClC_6H_4	Benzene, hexahedral prisms; petroleum ether, cubes	74.0	70—72	2.61	$C_{20}H_{17}O_5NSPCl_3$	2.68
(V)	$C_6H_5CH_2$	p-ClC_6H_4	Alcohol, rhombohedra; petroleum ether, cubes	75.5	132—133	2.34	$C_{25}H_{19}O_5NSPCl_3$	2.42
(VI)	C_2H_5	p-$NO_2C_6H_4$	Benzene, fine needles	65.2	108—110	9.90	$C_{20}H_{17}O_{11}N_4SP$	10.10

TABLE 2

Diaryl Esters of Alkylsulfonamidophosphoric Acids of the Type $RSO_2NHPO(OAr)_2$ (VII)

Substance no.	R	Ar	From what crystallized, form of crystals	Yield (in %)	Melting point	Found equiv.	Empirical formula**
—	CH_3	C_6H_5	CCl_4, long needles	43.3	96—98°	0.99, 1.00	$C_{13}H_{14}O_5NSP$
—	C_2H_5	C_6H_5	CCl_4, fine prisms	77.2	117—119	1.01, 1.01	$C_{14}H_{16}O_5NSP$
—	iso-C_3H_7	C_6H_5	CCl_4, fine prisms	86.3	140—142	1.01, 0.99	$C_{15}H_{18}O_5NSP$
—	n-C_4H_9	C_6H_5	CCl_4, fine needles	76.7	109—110	0.98, 1.00	$C_{16}H_{20}O_5NSP$
—	$C_6H_5CH_2$	C_6H_5	Water (precipitate), fine prisms	89.3	147—148	1.00, 1.00	$C_{19}H_{18}O_5NSP$
VIII	CH_3	p-ClC_6H_4	Ether, Rhombohedra	72.3 *	58—60	1.07, 1.06	$C_{13}H_{12}O_5NSPCl_2$
—	C_2H_5	p-ClC_6H_4	Water (precipitate), rectangular plates	90.0	133—135	1.01, 1.04	$C_{14}H_{14}O_5NSPCl_2$
—	$C_6H_5CH_2$	p-ClC_6H_4	Water (precipitate), fine prisms	73.8 *	149—151	0.99, 1.02	$C_{19}H_{16}O_5NSPCl_2$
IX	C_2H_5	p-$NO_2C_6H_4$	Alcohol, long prisms	78.9	166—167	0.98, 1.00	$C_{14}H_{14}O_9N_3SP$

* Yields from the synthesis from the dichlorides of the corresponding alkylsulfonamidophosphoric acids. All other yields for preparation by saponification of substances (I).

** Calculated equiv.: 1.0.

EXPERIMENTAL

General method for preparing triaryloxyphosphazosulfonalkyls (I). 0.03 g-molecules of carefully dried and ground sodium phenolate was moistened with 5 ml of dry benzene and a solution of 0.01 g-molecule of the corresponding trichlorophosphazosulfonalkyl in 20 ml of benzene was added with stirring. To complete the reaction, the mixture was heated on the boiling water bath for 30 min. In preparing (V) the heating lasted 4 hrs, and for (VI), 2 hrs. The benzene was distilled off in a vacuum and the syrupy residue was treated with 80-100 ml of water. With this treatment, all the substances (I) precipitated as heavy colorless rectangular plates which were filtered, washed with water, dried, and recrystallized (see Table 1). (II) precipitated as a thick oil which was extracted with benzene. The benzene extract was washed with 0.5 N sodium hydroxide solution, dried over sodium sulfate, and the benzene was distilled off in a vacuum at 50°. It was also possible after the reaction had been carried out to filter out the sodium chloride and distill off most of the benzene in a vacuum. When the solution was cooled, all the substances (I) precipitated as crystals (needles or prisms). This method was particularly suitable for (VI) which was difficultly soluble in cold benzene, and also for (III) and (IV).

General method for preparing diaryl esters of alkylsulfonamidophosphoric acids (X) by saponification of (I). A mixture of 0.01 g-molecule of the corresponding (I), 100 ml of alcohol, and 40 ml of 1 N aqueous solution of sodium hydroxide was heated on the water bath for 1 hr. The alcohol was distilled off in a vacuum, the water solution was filtered, and hydrochloric acid was added to an acid reaction to Congo paper. Substances (VII) then precipitated; they were filtered, dried, and, if necessary, recrystallized (see Table 2).

(IX) was obtained by boiling a solution of 0.003 g-molecule of (VI) in 30.0 ml of 96% alcohol for 10 min. The alcohol was distilled off in a vacuum, and the crystalline precipitate was washed with water and ether.

General method for preparing diaryl ethers of alkylsulfonamidophosphoric acids from alkylsulfonamidophosphoric acid dichlorides and sodium arylates. To a solution of 0.01 g-molecule of the dichloride of the corresponding alkylsulfonamidophosphoric acid in 100 ml of benzene was added 0.03 g-molecule of sodium arylate and the mixture was heated to boiling for 1 hr under reflux. The benzene was distilled off in a vacuum on a boiling water bath, the residue was dissolved in water, the solution was filtered and acidified with hydrochloric acid to an acid reaction to Congo. Substances (VII) precipitated and were filtered, washed with water, and dried. Substances (VII) obtained in this manner were usually entirely pure and did not have to be recrystallized. (VIII) which was comparatively easily soluble in water was extracted by ether after addition of acid.

SUMMARY

We have obtained triaryloxyphosphazosulfonalkyls and diaryl esters of alkylsulfonamidophosphoric acids and described their properties.

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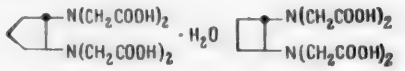
SUBSTANCES WITH COMPLEX FORMING ABILITY

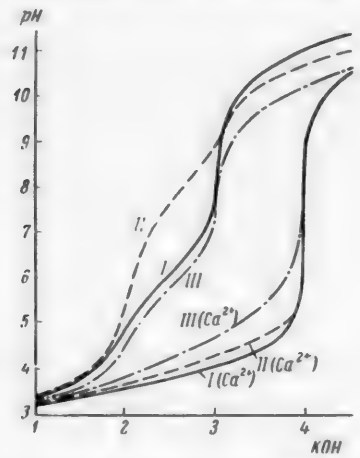
II. TRANS-1,2-DIAMINOCYCLOPENTANE-N,N,N',N'-TETRAACETIC ACID AND TRANS-1,2-DIAMINOCYCLOBUTANE-N,N,N',N'-TETRAACETIC ACID

V. G. Iashunskii

In a previous communication [1] we showed that the widely known "Complexon-IV," 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (I) has a trans-configuration. In order to study the effect of the structure of complexons on their complex forming power, we synthesized the undescribed close analogs of (I), trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid (II) and trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic acid (III). Acid (II) crystallizes with 1 molecule of water of crystallization which is not removed by heating in a vacuum to 100°. Acid (III) contains no water of crystallization.



(II) (III)



Curve of potentiometric titration of the tetra-acids (I), (II), and (III) in absence and presence of Ca^{2+} ions (amount of KOH in g-moles per 1 g-mole of tetra-acid).

Both tetra-acids were obtained by condensation of the corresponding diamino dihydrochlorides with monochloroacetic acid in the presence of alkali. Trans-1,2-diaminocyclopentane dihydrochloride was synthesized starting from ethyl cyclopentanone-2-carboxylate by nitration, oxime formation, and reduction of the resulting dioxime with metallic sodium in alcohol [2]. Trans-1,2-diaminocyclobutane dihydrochloride was obtained by the Curtius reaction from the dihydrazide of trans-cyclobutane-1,2-dicarboxylic acid, which was prepared from the corresponding diester [3].

Potentiometric titration of both tetra-acids in the absence and presence of calcium ions showed that these complexons resembled (I) in properties and also gave simple internal complex compounds, especially with Ca, of the composition CaX^{2-} (X is the tetra-acid residue). In the figure we give the curves for the potentiometric titration of (II) and (III), and for comparison, of (I). The data of the potentiometric titrations allows us to calculate [1] the apparent dissociation constants and stability constants of the Ca complexes of the complexons which we synthesized. In Table 1 for comparison we give also the corresponding values for (I) and for ethylenediamine-N,N,N',N'-tetraacetic acid (IV).

The results allow us to draw some conclusions as to the effect of structure of these complexons on ability to form complexes. If we compare the values of the stability constants of the Ca complexes of (IV), (I),(II), and (III), we can assume that to a large extent, two factors allow an increased stability of similar inner complex metallo-rings: closeness of the amino groups in the diamine molecule and absence of free rotation of these relative to the C_1-C_2 bond. In (IV) there is the maximum possible closeness of amino groups, but limitation of free rotation is absent. In (I) the cyclohexane ring permits closeness of the amino groups; the possibility of shifting of these

TABLE 1

Complexons	Reciprocal of logarithm of apparent dissociation constant				Logarithm of stability constant of Ca complex
	pK_1	pK_2	pK_3	pK_4	
(I)	2.7	3.6	6.15	11.65	12.5
(II)	2.4	3.3	7.56	10.80	12.2
(III)	2.7	2.8	5.80	9.75	8.0
(IV)*	1.996	2.672	6.161	10.262	10.59

* Data taken from the work of Schwarzenbach and Ackermann [4].

groups relative to each other is considerably decreased, but it does occur, since the six-membered ring can exist in the form of the "bath" and the "chair." Actually, the stability of the Ca complex of (I) compared to that of (IV) is considerably increased. In (II) the plane of the cyclopentane ring allows a distance of the amino groups from each other, but they become firmly held. As the experimental data with Ca^{2+} show, (I) and (II) have about the same complex forming ability. In (III) we find a still greater distance for the amino groups, and the absence of any free rotation. The potentiometric titration in the presence of Ca^{2+} shows that the value of the stability constant for the Ca complex of (III) is considerably lower than for (I) and even for (IV).

In a later study we shall investigate these regularities in the cis-series.

EXPERIMENTAL

Trans-cyclobutane-1,2-carboxylic acid dihydrazide [3]. 9.15 g of diethyl trans-cyclobutane-1,2-dicarboxylate (b. p. 126-127° at 17 mm, $d^{20}D$ 1.4406) was heated with 11.2 of hydrazine hydrate for 8 hrs at 130-135°. The resulting precipitate was treated with hot anhydrous ethyl alcohol and after cooling, this was filtered. After recrystallization from 50% ethyl alcohol, 5.65 g of the hydrazide was obtained, melting at 221-222°.

Trans-1,2-diaminocyclobutane dihydrochloride. 5.25 g of the dihydrazide was dissolved in 21 ml of 10% hydrochloric acid, 60 ml of ether was added, and with stirring at 18-20° a solution of 4.2 g of sodium nitrite in 9 ml of water was gradually added. The ether layer was separated, the water layer was twice extracted with 20 ml of ether, and after the ether solution was dried for 10-15 min over calcium chloride, 30 ml of anhydrous ethyl

TABLE 2

Tetraacid (II)			Tetraacid (III)		
KOH (mole/1 mole II)	conc. ($\times 10^{-4}$)	[H]	KOH (mole per mole III)	conc. ($\times 10^{-4}$)	[H]
0.427	9.92	$1.15 \cdot 10^{-3}$	1.372	9.99	$5.01 \cdot 10^{-4}$
0.854	9.88	$6.92 \cdot 10^{-4}$	1.476	9.98	$3.98 \cdot 10^{-4}$
0.960	9.87	$6.03 \cdot 10^{-4}$	1.580	9.97	$3.24 \cdot 10^{-4}$
1.068	9.86	$5.01 \cdot 10^{-4}$			
Titration in presence of Ca^{2+} (0.01 M)					
2.695	9.84	$6.31 \cdot 10^{-5}$	2.762	9.76	$1.95 \cdot 10^{-5}$
2.802	9.83	$6.03 \cdot 10^{-5}$	2.975	9.73	$1.38 \cdot 10^{-5}$
2.908	9.82	$5.01 \cdot 10^{-5}$	3.185	9.72	$9.33 \cdot 10^{-6}$

Note. Titration was carried out with 0.1 N KOH at 20° (μ = 0.1). $pK_3' + pK_4'$ = 8.1 for tetra-acid (II) and $pK_3' + pK_4'$ = 9.5 for tetra-acid (III).

alcohol was added. The ether was distilled off and the residue was heated to boiling for 1 hr; then 25 g of potassium hydroxide and 75 ml of methyl alcohol were added and boiling was continued for 2 hrs more. The mixture was then distilled with steam, the distillate was acidified with hydrochloric acid and evaporated dry. We obtained 3.18 g (67%) of trans-1,2-diaminocyclobutane dihyrochloride which was recrystallized from hydrochloric acid.

Found %: Cl 44.62. $C_4H_{10}N_2 \cdot 2HCl$. Calculated %: Cl 44.57.

Trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic acid. To 8.9 g of monochloroacetic acid neutralized with 13.5 ml of 7 N sodium hydroxide solution we added 3.0 g of trans-1,2-diaminocyclobutane dihydrochloride; the mixture was heated on the boiling water bath and 18 ml of 7 N sodium hydroxide solution was added with stirring. The addition of alkali was so conducted that tests constantly gave a blue color on thymolphthalein paper. After 3 hrs the mixture was acidified with concentrated hydrochloric acid to a pH of 1-2, and the precipitate was recrystallized from a large amount of water. We obtained 2.83 g of pure tetra-acid.

Found %: C 45.13; H 5.71; N 8.86. M 318.1 (on titration with $CaCl_2$ in the presence of murexide). $C_{12}H_{18}O_8N_2$. Calculated %: C 45.28; H 5.70; N 8.80. M 318.3.

Trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid was obtained in a manner analogous to the above from trans-1,2-diaminocyclopentane dihydrochloride; the yield after reprecipitating the acid from alkaline solution was 56%.

Found %: C 44.76; H 6.25; N 8.27. M 349.6 (on titration with $CaCl_2$ in the presence of murexide). $C_{13}H_{20}O_8N_2 \cdot H_2O$. Calculated %: C 44.56; H 6.33; N 8.00. M 350.3.

When it was heated in a vacuum to 100° the monohydrate did not lose a molecule of water. Potentiometric determination and calculation of dissociation constants was carried out by the method of Schwarzenbach (see [1]). As an example, in Table 2 we give the results of one of the parallel titrations for the tetra-acids (II) and (III).

SUMMARY

We have synthesized the previously undescribed complexons: trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid and trans-1,2-diaminocyclobutane-N,N,N',N'-tetraacetic acid for which we determined the apparent dissociation constants and the stability of the Ca complexes.

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CYANOETHYLATION OF ARYL SULFONAMIDES

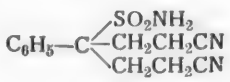
A. E. Kretov and N. P. Romazanovich

The study of the chemical properties of benzenesulfonamide and its derivatives has great interest for the discovery of new sulfonamide compounds and for an explanation of their pharmacological action [1]. In recent times the cyanoethylation reaction has been widely used, taking place when acrylonitrile acts on substances with a mobile hydrogen atom. A series of reviews on cyanoethylation have appeared [2]. Acrylonitrile has acted on halides, amines, compounds of the type of malonic ester, and others. There have been studies on cyanoethylation of acids and their derivatives, esters, nitriles, and amides [3-5]. The synthetic possibilities of this reaction have only been touched upon, but already the opportunities for its practical use are clear.

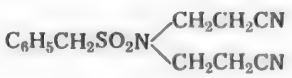
The literature mentions that when the products of cyanoethylation of amines are hydrolyzed, substances are obtained which have physiological activity [6, 7]. As is known, the most active sulfonamides contain the benzenesulfonamide grouping with substitution of the hydrogen atoms in the amide group [8]; therefore we studied the cyanoethylation reaction of benzenesulfonamide and its derivatives.

Benzenesulfonamide in the presence of alkaline agents reacts with acrylonitrile at 100° to form the dicyanoethyl derivative [9, 10].

Among the substituted benzenesulfonamides, to judge them from the literature data, benzylsulfonamide is cyanoethylated. The resulting product was assigned structure (I) [5]. However, as was shown later [11] cyanoethylation occurs on the amide group with formation of compound (II).



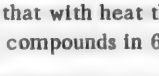
(I)



(II)

The mechanism of reaction of combining acrylonitrile with benzenesulfonamide and its derivatives differs from the mechanism of cyanoethylation of the amides of carboxylic acids [12]. The latter react sluggishly with acrylonitrile. Thus, acetamide in the presence of alkali gives products of mono- and dicyanoethylation on the amide group [9, 10]. It is interesting to observe that with heat the dicyanoethyl derivatives with acetamide disproportionate with formation of monocyanoethyl compounds in 62% yield [9].

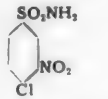
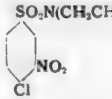
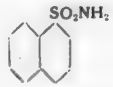
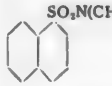
When benzenesulfonamide undergoes cyanoethylation it is important to consider the combination of the benzene ring with sulfo- and amino groups. A positive charge occurs on the nitrogen atom as a result of the electrophilic action of the sulfur atom and the shift of free electrons; this makes detachment of the proton easy (A).



(A)

This splitting is stronger in an alkaline medium where a state of dynamic equilibrium is established.

Cyanoethylation of Arylsulfonamides

Starting substance	Resulting substance	Melting point	Kjeldahl nitrogen analysis [13]		Yield (in %)	Catalyst
			found	calc.		
$C_6H_5SO_2NH_2$	$C_6H_5SO_2N(CH_2CH_2CN)_2$	92°	16.71	15.96	66.2	NaOH
$p\text{-}CH_3C_6H_4SO_2NH_2$	$p\text{-}CH_3C_6H_4SO_2N(CH_2CH_2CN)_2$	104—105	15.09	15.16	77.3	NaOH
	$p\text{-}CH_3C_6H_4SO_2NHCH_2CH_2CN$	55—56			15.7	
$p\text{-}ClC_6H_4SO_2NH_2$	$p\text{-}ClC_6H_4SO_2N(CH_2CH_2CN)_2$	133	13.5	14.1	70	NaOH
$p\text{-}NH_2C_6H_4SO_2NH_2$	$p\text{-}NH_2C_6H_4SO_2N(CH_2CH_2CN)_2$	145	20.1	20.14	57.7	NaOH
					66.9	Rodionov Catalyst
$p\text{-}CH_3CONHC_6H_4SO_2NH_2$	$p\text{-}CH_3CONHC_6H_4SO_2N(CH_2CH_2CN)_2$	131—132	17.66	17.46	75	Rodionov Catalyst
$p\text{-}NH_2C_6H_4SO_2NHC_5H_4N$	$p\text{-}NH_2C_6H_4SO_2N(CH_2CH_2CN)C_5H_4N$	165	18.23	18.54	73	Rodionov Catalyst
$p\text{-}NO_2C_6H_4SO_2NH_2$	$p\text{-}NO_2C_6H_4SO_2N(CH_2CH_2CN)_2$	150			67.8	NaOH
		160—162			64.3	NaOH
		152	13.36	12.84	65.1	NaOH
		210	13.33	12.84	58.4	NaOH

Spectrographic study of benzenesulfonamide in an alkaline medium at ratio of molar concentrations 2 : 1 shows the splitting of two protons and formation of a doubly charged anion of benzenesulfonamide $[C_6H_5SO_2\ddot{N}:]^{=}$ [1]. This evidently explains the catalytic action of the sodium hydroxide on the cyanoethylation of benzenesulfonamide and also the difficulty of isolating the products of monocyanoethylation. At a molar ratio of benzenesulfonamide and sodium hydroxide of 1 : 3 under our conditions it is possible also to form the singly charged anion of benzenesulfonamide $[C_6H_5SO_2NH]^{-}$.

The reaction of cyanoethylation of benzenesulfonamide was carried out as follows. 5.2 g of benzenesulfonamide dissolved in 20 ml of dioxane was heated with 0.5 g of sodium hydroxide on the water bath under reflux, with gradual addition of 5 ml of acrylonitrile. Heating was continued 1.5-2 hrs and the reaction mixture allowed to stand for a day. The dicyanoethylation product was easily isolated after decomposition of the reaction mixture with water. Dicyanoethylbenzenesulfonamide recrystallized from ethanol appeared as white needles, melting at 92°. If the solvent (dioxane) was distilled from the reaction mixture in a vacuum, then along with the dicyanoethylbenzenesulfonamide we obtained a small amount of an oil which crystallized when it stood in a vacuum desiccator over sulfuric acid. When the cyanoethylation reaction was carried out in anhydrous ethanol, the amount of this oil increased.

We carried out cyanoethylation of the following derivatives of benzenesulfonamide with nucleophilic substituents: p-toluenesulfonamide, p-chlorobenzenesulfonamide, p-aminobenzenesulfonamide, p-acetylaminobenzenesulfonamide, and sulfidine. The resulting cyanoethylated derivatives of benzenesulfonamide and their analytical data are shown in the table.

The cyanoethylation reaction with p-toluenesulfonamide was carried out in dioxane and ethanol solutions under the conditions for cyanoethylation of benzenesulfonamide. After 4 hr heating of the reaction mixture in ethanol solution we obtained the products of di- and monocyanoethylation of p-toluenesulfonamide. The monocyanoethylation product was easily separated and formed in greater yield than in the case of benzenesulfonamide. This was explained by the effect of the methyl group on the union of the sulfonamide group with the benzene ring and the greater possibility of forming a singly charged anion of benzenesulfonamide.

When p-toluenesulfonamide and its dicyanoethylation product were heated in anhydrous alcohol in the presence of sodium hydroxide, a disproportionation reaction occurred and the product of monocyanoethylation of p-toluenesulfonamide, melting 55-56°, was formed.

For the cyanoethylation of p-aminobenzenesulfonamide we used sodium hydroxide and the Rodionov catalyst as catalysts; the latter we obtained from methyl p-aminobenzenesulfonate [14]. In both cases we obtained the same dicyanoethylation product, but with the Rodionov catalyst reaction occurred more smoothly and the yield was higher. Analysis for nitrogen showed that two atoms of hydrogen were cyanoethylated in the molecule of p-aminobenzenesulfonamide. To establish the mechanism of the reaction, which in this case might have occurred on the amido or the amino group, we cyanoethylated substituted benzenesulfonamides, the acetylated streptocide and sulfidine, in pyridine solution (see table).

Cyanoethylation of p-aminobenzene-N-dimethylsulfonamide showed that reaction did not occur under these conditions.

p-Aminobenzene-N-dimethylsulfonamide was prepared by reduction of p-nitrobenzenedimethylsulfonamide [15].

The N-methylamide of acetylsulfanilic acid, $CH_3CONHC_6H_4SO_2NHCH_3$, was cyanoethylated on the sulfonamide group, but the N,N-dimethyl amide of acetylsulfanilic acid $CH_3CONHC_6H_4SO_2N(CH_3)_2$ did not cyanoethylate. Cyanoethylation does not occur on the carbamide group [16].

Among the derivatives of benzenesulfonamide with electrophilic substituents we cyanoethylated p-nitrobenzenesulfonamide, prepared from p-nitrochlorobenzene [17, 18]. Reaction was carried out in dioxane in the presence of the Rodionov catalyst with longer heating of the reaction mixture.

The literature describes a series of cyanoethylation products of chlorine substituted aromatic compounds, which were investigated as insecticides [19]. Because of this interest we prepared 1-chloro-2-nitro-4-benzenesulfonamide. Strong reaction occurred in the presence of Rodionov catalyst with formation of the dicyanoethylation product.

SUMMARY

1. In the cyanoethylation reaction with acrylonitrile we have obtained 10 new compounds, not described in the literature.

2. A study of the mechanism of this reaction shows that replacement of hydrogens by the cyanoethyl group under the conditions described occurs only on the amide group. Reaction does not occur on the amino group.

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* Original Russian pagination. See C. B. translation.

** In Russian.

SYNTHESIS OF THE DIETHYLENEIMIDE OF 4-METHYLURACIL 5-METHYLENE PHOSPHINIC ACID

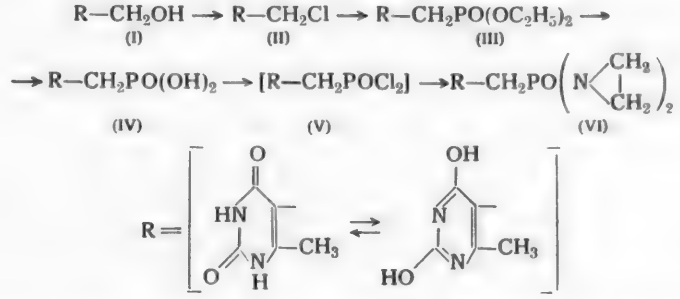
A. Ia. Berlin and M. N. Vasil'eva

In seeking new chemical agents against malignant neoplasms the attention of many investigations has turned to substances with so-called "alkylating" action, substances which contain β,β'-dichlorodiethylamino and ethylene imino groups, etc.

The recently synthesized p-(β,β'-dichlorodiethylamino)-phenylalanine hydrochloride ("sarcolysine") [1] is one of the most interesting preparations of this type, since its clinical use has for the first time permitted effective action against some forms of true human tumors and their metastases [2]. In the sarcolysine molecule there is an active alkylating dichlorodiethylamino group combined with a phenylalanine residue which plays an important part in protein metabolism. This fact leads us to seek a substance with analogous structural characteristics which might have an anti-cancer action also for other types of malignant tumors.

Starting from these ideas, we were interested in synthesizing the diethylene imide of 4-methyluracil 5-methylenephosphinic acid (VI), which contains the active cytotoxic diethylenephosphoramide group along with a residue of a uracil derivative which, like some of its other derivatives, enters the composition of nucleic acids.

The synthesis was carried out according to the following scheme.



The transformation of 4-methyl-5-hydroxymethyluracil ("pentoxyl") (I) into the corresponding chloride (II) required careful choice of reaction conditions, since the chlorine could replace not only the hydroxyl group in the side chain but also the hydroxyl of the lactone form of the uracil ring [3]. It was shown that the best method was to carry out reaction between pentoxyl and thionyl chloride in cold chloroform in the presence of 1 mole of pyridine. Excess pyridine caused considerable tarring.

The resulting 4-methyl-5-chloromethyluracil (II) melted about 225° (with decomposition) with a rate of heating of 10° per minute. With slower heating (2° per min) the substance gradually darkened but did not melt up to 345°. Endicott and Johnson [4] synthesized this compound from 4-methyluracil and monochloromethyl ether; without mentioning the effect of rate of heating on melting point, they observed that it turned yellow at 225° and melted with decomposition at 330-335°. We can assume that Endicott and Johnson apparently had the same substance but determined its melting point with a different rate of heating. It should be remarked that the melting point given by Johnson and Chernoff [5] for the isomeric 4-chloromethyl-5-methyluracil, 243°, is close

to that established by us for substance (II). When we repeated the synthesis described by Endicott and Johnson [4] we obtained a complex mixture of substances which easily altered, and which was very difficult to separate. This led us to work out the other synthesis of (II) starting with pentoxyl.

Next, by the action of triethyl phosphite on 4-methyl-5-chloromethyluracil (II), by the Arbuzov reaction, we isolated the diethyl ester of 4-methyluracil 5-methylenephosphinic acid (III). Heating the diethyl ester (III) with hydrochloric acid gave a good yield of the corresponding 4-methyluracil 5-methylenephosphinic acid (IV).

The transformation of the phosphinic acid (IV) into its dichloride (V) also required care in carrying out the reaction in view of the above-mentioned possibility of undesired substitution. However, even with very mild conditions the reaction does not go in a single direction and a mixture of different substances results, from which we were unable to separate the chloride (V) in pure form. Nonetheless, the fact of formation of 4-methyluracil 5-methylenephosphinic acid dichloride was established, since reaction of the mixture of substances with anhydrous ethyl alcohol gave 21% of the diethyl ester (III) (after recrystallization).

Analogously, the action of ethylene imine on the reaction product from the phosphinic acid (IV) and thionyl chloride [6] gave the diethylene imide of 4-methyluracil 5-methylenephosphinic acid (VI) as a crystalline substance which changed when heated in a capillary but showed no definite melting point.

We consider it a pleasure to express our gratitude to M. I. Kabachnik and T. Ia. Medved for their advice in our work.

EXPERIMENTAL

4-Methyl-5-chloromethyluracil (II). To a mixture of 10 g of 4-methyl-5-hydroxymethyluracil (pentoxyl), 5.1 ml of dry pyridine and 100 ml of dry chloroform was added a solution of 10 g of thionyl chloride in 15 ml of the same solvent over a period of 30 min with stirring and ice cooling. The reaction temperature did not exceed 20°. After 3 hrs of stirring, the reaction mixture was filtered, the precipitate was well washed with dry chloroform and air dried until the odor of SO_2 vanished. Weight 8 g. After 3 recrystallizations from dioxane we obtained 5.1 g of crystalline substance melting at ~ 225° (with decomposition) with a rate of heating of 10° per min.

Found %: C 41.2, 41.5; H 4.2, 4.2; N 16.5, 16.5; Cl 20.2, 20.4. $C_6H_7O_2N_2Cl$. Calculated %: C 41.2; H 4.0; N 16.0; Cl 20.4.*

Diethyl 4-methyluracil 5-methylenephosphinate (III). In a 50 ml flask with reflux condenser and calcium chloride tube was placed 4 g of (II) and 4.3 g of triethyl phosphite (calculated 3.8 g). The mixture was placed in an oil bath previously heated to 130°. At a bath temperature of 160° reaction began with a violent evolution of gas. When evolution of ethyl chloride was complete the flask was heated for another 20 min at 150-155°. The result of the reaction was an oil which solidified when stirred with absolute ether. The solid mass was well washed with ether and dried. Weight 3.8 g, m. p. 97-102°. For purification the substance was dissolved in 12.0 ml of dry benzene at 40-55° and fractionally precipitated by the addition of excess petroleum ether. An oily substance first began to precipitate, and then crystals which were recrystallized from a mixture of benzene and petroleum ether (4 : 1). We obtained 2.2 g of diethyl 4-methyluracil 5-methylenephosphinate., m. p. 106-107.5°. The substance was well soluble in benzene, chloroform, alcohol, dioxane, and water; insoluble in ether and petroleum ether.

Found %: C 43.5, 43.3; H 6.2, 6.5; N 9.8, 10.1; P 11.06, 11.02. $C_{10}H_{17}O_5N_2P$. Calculated %: C 43.5; H 6.2; N 10.2; P 11.2.

4-Methyluracil 5-methylenephosphinic acid (IV). 0.5 g (III) in 10 ml of concentrated hydrochloric acid was boiled for 5 hrs. After removal of excess hydrochloric acid in a vacuum we obtained 0.4 g of 4-methyluracil 5-methylenephosphinic acid, m. p. 280°. It was recrystallized from dilute ethyl alcohol to give 0.3 g (IV) with m. p. 282-284°.

Found %: C 32.5, 32.5; H 4.1, 4.1. $C_6H_9O_5N_2P$. Calculated %: C 32.7; H 4.1.

*All the analyses were carried out in the Analytical Chemistry Laboratory of our Institute.

Diethylene imide of 4-methyluracil 5-methylenephosphonic acid (VI). 5 g of (IV) in 50 ml of thionyl chloride was heated at 50° for 30 min. After removing the excess thionyl chloride in a vacuum at room temperature, the dry residue was treated with 50 ml of dry benzene. A solution of 2.5 ml of ethylene imine and 7.5 ml of triethylamine in 20 ml of dry benzene was added from a dropping funnel with stirring. The flask was then cooled with ice water so that the bath temperature did not exceed 10°. After all the solution had been added, the mixture was stirred for 2.5 hrs more and allowed to stand for 16 hrs at 0-5°. The precipitate was filtered off. The solvent was removed from the filtrate in a vacuum in a stream of nitrogen at a bath temperature not above 30° and the solid residue was recrystallized from dry benzene which was not heated above 45°. We obtained 1.5 g of the diethylene imine of 4-methyluracil 5-methylenephosphinic acid. In the melting point determination the substance began to darken at about 120° and on further heating gradually changed and decomposed at 268°.

Found %: C 44.1, 44.2; H 5.5, 5.6; N 20.1, 20.1. $C_{10}H_{15}O_3N_4P$. Calculated %: C 44.4; H 5.5; N 20.7.

SUMMARY

Starting from 4-methyl-5-hydroxymethyluracil (pentoxyl) through 4-methyl-5-chloromethyluracil we synthesized the diethyl ester of 4-methyluracil 5-methylenephosphinic acid and the free 4-methyluracil 5-methylene phosphinic acid. From the latter we obtained the diethylene imine of 4-methyluracil 5-methylenephosphinic acid.

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STUDIES IN THE FIELD OF SYNTHESIS AND POLYCONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

I. SYNTHESIS OF N,N'-DIALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

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The value of polyamides for different branches of industry is widely known.

In recent decades, works have begun to appear in the literature concerning the question of modifying the properties of polyamides to give them more elasticity, softness, and hydrophilic properties, while retaining a series of other valuable properties. Such modifications can be brought about by several methods. In particular, the method of N-alkylation has wide possibilities; yet in the literature it has not been sufficiently reported.

To obtain N-alkylated polyamides with varying degrees of substitution and also with different substituted radicals it is necessary to have methods for the synthesis of the corresponding monomers (N-alkylated hexamethylenediamine) which will guarantee a sufficiently pure product, the possibility of introducing radicals with different structures, and also the possibility of preferentially directing the reaction toward N-mono- or symmetrical N,N'-dialkylation. It would also be desirable that the method be simple, based on available compounds and that it permit the carrying out of the reaction on a large scale. Such a method is not now known. Methods are described in the literature for the synthesis of N,N'-dialkyldiamides by amination of the corresponding dibromides [1], and by hydrogenation of the dinitriles in the presence of methylamine [2]. Both methods lead to the formation of a mixture of products which are difficult to separate.

The reduction of Schiff bases of diamines described by Staudinger is complicated by the great instability of the aliphatic azomethines and leads to a low yield of the latter [3].

Since the polycondensation process requires monomers with a high degree of purity, the method of reductive alkylation of amines by aldehydes and ketones is of interest; this, according to the description [4], assures a high yield and a choice of reactions for getting secondary monoamines and satisfies the other requirements discussed above. The literature data relate entirely to monoamines. With regard to the reductive alkylation of diamines there is only one patent, which concerns obtaining N-monoalkyl derivatives [5].

The complexity and peculiarity of the reaction of alkylating diamines is connected with the presence of two active groups in the diamine molecule. In this connection, one of the problems of our investigation is to work out a synthesis of N,N'-dialkyl derivatives of hexamethylene diamine based on reductive alkylation and proceeding according to the following scheme

$$R{-}NH_2 + O{=}C\begin{matrix}R'\\R''\end{matrix} \xrightarrow[-H_2O]{H_2} R{-}NH{-}CH\begin{matrix}R'\\R''\end{matrix}$$

R' and R" are alkyl radicals or H

We studied the effect of a series of factors on reaction rate and yield of N,N'-dialkyl derivatives of hexamethylene diamine.

Effect of solvents. The reaction carried on without solvent was unsatisfactory, since the exothermic nature of the process caused strong tarring. The viscous consistency of the mixture also prevented even distribution of the catalyst and worsened the conditions of hydrogenation. We used as solvents substances which dissolved both the diamine and the carbonyl compound well. The results are shown in Table 1.

TABLE 1

Effect of Solvents on Course of Reductive Alkylation of Hexamethylenediamine

Alkylating compound	Solvent	Duration of 50% reaction (in min)	Limiting extent of reaction (in %)	Yield of N,N'-dialkyl derivative (in %)
Butyraldehyde	Anhydrous alcohol	15—16	100	87
	96% alcohol	15—17	100	85
	Dioxane	25—30	82	70
	Water	27—30	70	50—55
Acetone	Anhydrous alcohol	8—10	100	96
	96% alcohol	8—10	100	93
	Dioxane	15—20	90	80
	Water	15—20	96	66

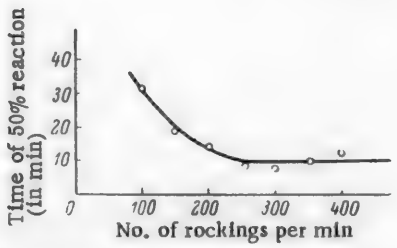

Fig. 1. Relation of rate of reduction of a mixture of hexamethylenediamine—acetone to conditions of mixing.

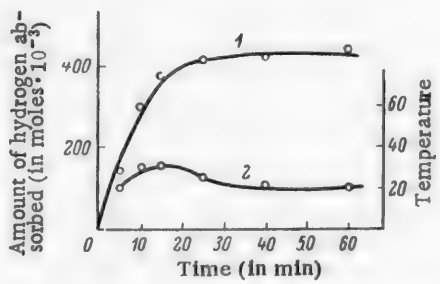

Fig. 2. Change in temperature during reduction of a mixture of hexamethylenediamine—butyraldehyde. 1) Amount of hydrogen absorbed, 2) temperature.

The best solvent was ethyl alcohol. The use of water is limited not only by the fact that it does not dissolve a large number of carbonyl compounds, but also because the products of alkylation of hexamethylenediamine are solid, water-insoluble hydrates. The formation of a solid phase makes hydrogenation difficult and shifts the reaction toward formation of monosubstitution products.

Effect of mixing. For a determination of the reaction kinetics we carried out experiments with a different amount of rocking the ampules (alkylation compound, acetone; initial pressure 110 atmos). As Fig. 1 shows, under the conditions which we used, the shortest time is reached at 250 rockings per min. In all further experiments we used 280-300 rockings per min.

Effect of temperature. Reductive alkylation of hexamethylenediamine goes exothermally (Fig. 2) with sufficient speed and to the end at room temperature. Increasing the temperature (120-130°) is advisable when alkylating with highly branched ketones (diisobutyl ketone) since at lower temperatures these almost do not react, as Fig. 3 shows.

Effect of catalyst. For this reaction we used the ordinary hydrogenation catalysts. The results are shown in Table 2.

Effect of concentration and ratio of reagents. The concentration of diamine and alkylating agent under the experimental conditions does not affect the reaction rate within definite limits (~ 30%). Further increase in concentration leads to decreased yield of N,N'-dialkylation products due to partial tarring and increase in high-boiling fractions (Table 3).

The ratio of reaction components has the following effects. With insufficient alkylating agent we get a mixture of N-mono- and N,N'-disubstituted diamine. With the theoretical ratio of components almost no monosubstituted diamine is obtained. An excess of alkylating agent in the case of use of acetaldehyde or propion-

TABLE 2

Relation of Reductive Alkylation Reaction of Hexamethylenediamine by Acetone to Nature of Catalyst

Catalyst	Weight of catalyst calculated as metal (in g)	Time of occurrence of 50% reaction (in min)	Extent of reaction (in %)	Yield of N,N'-dialkyl derivative based on starting diamine (in %)
Platinum black	0.185	8—10	100	93—96
Palladium on $BaSO_4$	0.200	25—30	90	75—80
Raney nickel	3.000	120	86	70

TABLE 3

Effect of Concentration of Reagents on Rate of Hydrogen Absorption and Yield of N,N'-Dialkylated Products

Alkylating compound	Conc. on diamine (in M)	Absorption of H_2 in 20 min (in mmole)	Extent of reaction (in %)	Yield of N,N'-dialkyl derivative based on starting diamine (in %)
Acetone	1.0	161	100	93
	2.0	165	100	95
	3.7	115	79	68
Butyraldehyde	1.0	77	100	84
	2.0	77	100	85
	3.4	43	72	54

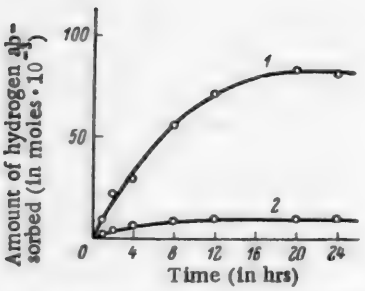

Fig. 3. Rate of reduction of a mixture of hexamethylenediamine—diisobutyl ketone at different temperatures. 1) at 130°, 2) at 20°.

aldehyde causes a lowered yield of N,N'-dialkyl derivative due to formation of products of a greater degree of alkylation. In the case of use of ketones and higher aldehydes their excess did not affect the yield of the chief reaction products (under the conditions described).

Since the separation of mixtures of N-mono- and N,N'-dialkyl and also tri- and tetra-substituted diamines is difficult, they were separated only into fractions which contained mixtures of mono-, di-, or tri- and tetraalkylated diamines. In each fraction the content of the components was calculated (on the basis of the determined total nitrogen in the given fraction) by the equation

$$xa + (100 - x)b = c \cdot 100,$$

where: x is the percent content (by weight) of the 1st component in the mixture (for example, the monosubstituted), a the theoretical percent content of N in the 1st component, b the theoretical percent content of nitrogen in the 2nd component (disubstituted diamine), c the percent content N in the fraction, found by analysis.

The resulting data are given in Table 4. With excess acetaldehyde and propionaldehyde we found an increased amount of tri- and tetrasubstituted diamines. When we used ketones and aldehydes with a C_4 chain no effect of excess alkylating compound was observed. This effect is evidently explained by the increasing steric effects of the substituting groups because of the increasing length and branching of the chains. Such groups hinder further alkylation of the amino groups to tertiary amines.

Effect of structure of alkylating compound. The above optimum conditions for carrying out the reaction when alkylating with acetone and butyraldehyde were also used in the main with other carbonyl compounds. The only changes were in temperature regime and method of isolating the reaction products.

TABLE 4

Effect of Ratio of Reagents on Yield of N,N'-Dialkyl Hexamethylenediamines (based on taken diamine)

Alkylating compound	Molecular ratio of hexamethylenediamine and carbonyl compound	Yield		
		N-monoalkyl derivative (in %)	N,N'-dialkyl derivative (in %)	mixture of tri- and tetraderivatives (in %)
Acetone	1 : 1	15	34	none
	1 : 2	none	93	none
	1 : 3	none	90	none
Butyraldehyde	1 : 1	20	32	none
	1 : 2	none	86	none
	1 : 3	none	82	none
Propionaldehyde	1 : 1	18	36 *	none
	1 : 2	none	58 *	27
	1 : 3	none	37	52
Acetaldehyde	1 : 1	21	32 *	none
	1 : 2	—	41 *	13
	1 : 3	none	19	69

* Yield is lowered because of formation of unsymmetrical N-dialkyldiamine.

Thus, when we alkylated with acetaldehyde, in order to avoid tarring of the latter (which occurs intensively under reaction conditions without cooling) we cooled to −8 to −10° in the initial period of the reaction (when mixing the components). It was advisable to add the aldehyde to the diamine solution in a hydrogen atmosphere. When using propionic and isobutyric aldehydes we also recommend cooling (from 0 to −3°) in the initial period of the reaction, but when ketones are used this is not necessary. The use of higher temperatures in the alkylation of diisobutyl ketone has already been mentioned.

Isolation of the reaction products usually consists of the following steps: 1) distillation of the volatile products from the reaction mixture (solvent and excess carbonyl compound), 2) washing the ether solution with water to remove unreacted hexamethylenediamine, 3) drying the mixture after washing, 4) distillation in a vacuum (in an atmosphere of nitrogen) to remove the N,N'-dialkylation products.

The step of washing out the hexamethylenediamine can often be omitted, as for example in the case of alkylation by acetone and methyl ethyl ketone where reaction goes almost to completion. In the case of using acetaldehyde, washing is inadvisable because of the appreciable solubility in water of the dialkylation product. With higher aldehydes and ketones, when the alkylation reaction does not go to completion, washing out the diamine is necessary, since if this not done, isolation of a pure product by distillation is very difficult.

For the alkylation of hexamethylenediamine we used acetaldehyde, propionaldehyde, n-butyraldehyde, isobutyraldehyde; and acetone, methylethyl ketone, and diisobutyl ketone. We obtained a series of compounds which are described in Table 5.

EXPERIMENTAL

The experiments were carried out in a steel autoclave with a heater, capacity 150-200 ml, which was set in a shaking apparatus. The course of the reaction was controlled by the fall in pressure. The reaction mixture was analyzed for total nitrogen content, primary amines, and carbonyl groups. Separation of the reaction products was carried out by fractional distillation in a vacuum.

Alkylation with n-butyraldehyde. In the autoclave we placed a solution of 23.2 g of hexamethylenediamine in 50 ml of 96% alcohol, and then with ice cooling we added 28.8 g of n-butyraldehyde and 0.2 g of platinum oxide (prepared according to Adams). The autoclave was closed, and hydrogen was twice passed in under pressure to 50 atoms, then it was filled with hydrogen to a pressure of 150 atmos, and the apparatus was placed on the shaker at room temperature. Absorption of hydrogen was followed for 60 min to a final pressure

TABLE 5

N,N'-Dialkyl Derivatives of Hexamethylenediamine

Name of compound and its formula	Boiling point (pressure in mm)	d_4^{25}	n_D^{25}	Yield		Analytical data (in %)						MR_D	
						N (total)		NH *		found (by molecular wt.)			
				on starting diamine	on reacting diamine	found (Kjeldahl)	calc.	found (by acetylation)	calc.	found (Rast)	calc.	found	calculated
N,N'-Diethylhexamethylenediamine	101—105° (7)	0.825	1.4440	41	47	16.2	16.3	16.3	16.3	168	172	55.4	55.6
N,N'-Di-n-propylhexamethylenediamine	102—105 (2)	0.831	1.4451	58	64	14.0	14.0	13.9	14.0	196	200	64.2	64.8
N,N'-Diisopropylhexamethylenediamine**	110—112 (3)	0.816	1.4393	95	95	14.1	14.0	13.9	14.0	201	200	64.8	64.8
N,N'-Di-n-butylhexamethylenediamine	131—133 (3)	0.825	1.4479	87	90	12.2	12.3	12.4	12.3	238	228	73.9	74.1
N,N'-Diisobutylhexamethylenediamine	112—115 (2)	0.818	1.4481	85	86	12.5	12.3	—	—	220	228	74.0	74.1
N,N'-Dibutyl-2-hexamethylenediamine**	115—118 (2)	0.828	1.4475	90	90	12.5	12.3	—	—	232	228	73.5	74.1
N,N'-Di-(2,6-dimethylheptyl-4)-hexamethylenediamine**	183—184 (2)	0.835	1.4554	25	66	7.7	7.6	—	—	354	368	119.7	120.2

* The NH_2 group determined according to Van Slyke was absent in all the compounds.

** Obtained first.

of 30 atmos which corresponded to an absorption of 400 mmoles of H_2 (100%). After discharge of pressure and settling of the catalyst, the reaction mixture was analyzed for content of primary amino groups by the Van Slyke method, showing 2.4% NH_2-groups (of the starting amount). The alcohol was distilled from the reaction mixture, the residue was dissolved in 200 ml of ether, the unreacted diamine was washed out with 150 ml of water (in 25 ml portions) and was dried over K_2CO_3. After distilling off the ether the alkylation product was separated by distillation in a vacuum (in an atmosphere of nitrogen) from a flask with a rectifying column. Almost all the product came over at 128-132° (2-3 mm) and was obtained in the amount of 39.5 g (yield 87% on amount of diamine in the reaction). The analytical data for the resulting N,N'-di-n-butylhexamethylenediamine are given in Table 5.

Alkylation with acetone was carried out under the same conditions. To a solution of 23.2 g of hexamethylenediamine in 50 ml of alcohol was added (without cooling) 23.2 g of acetone and 0.2 g of catalyst. The fall in hydrogen pressure was from 150 to 30 atmos which corresponded to an absorption of 403 mmoles H_2 (101%) over 35 min. There were no primary amino groups in the mixture; therefore the mixture was distilled without washing after drying. Almost all the product passed over at 102-104° (2 mm) and was obtained in the amount of 38.3 g (yield 96%). The analytical data for the resulting compound are given in Table 5.

To confirm the structure of the resulting N,N'-diisopropylhexamethylenediamine we took its infrared spectrum* from 2 to 10 μ. In the spectrum we found bands at 3292 cm^{-1} which belonged to the N—H oscillation. At 1400-1800 cm^{-1} there was no absorption which showed the absence of the groups C=O, C=N, C=C, and NH_2 in the compound studied.

SUMMARY

1. On the basis of the reductive alkylation reaction we worked out a method for the synthesis of N,N'-dialkyl derivatives of hexamethylenediamine with various substituents, which assures a series of alkyl compounds in high yield.

2. The optimal conditions for the reaction are: ethyl alcohol as solvent, reagent concentration of 20-25% (of the diamine); ratio of diamine to carbonyl compound (in moles) 1 : 2; platinum black catalyst (0.1-0.05%); reaction temperature 20-25° (except in special cases); hydrogen pressure during the reaction 120-150 atmos.

3. We have studied and characterized seven N,N'-dialkyl derivatives of hexamethylenediamine, three of them synthesized for the first time.

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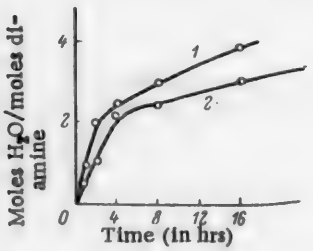
RESEARCH IN THE FIELD OF SYNTHESIS AND POLYCONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

II. THE SYNTHESIS OF N-MONOALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

The preparation of N-monosubstituted derivatives of hexamethylenediamine under conditions which preserve the special features of reduction alkylation [1], involves many difficulties. Reaction of the carbonyl compounds with the NH_2 group of either the free or monosubstituted diamine (present in solution) is equally probable, at least in the early stages of the reaction. This leads to the formation of a mixture of N-mono- and N,N'-dialkyl diamines that is difficult to separate and contains a considerable proportion of the disubstituted component, which lowers the yield of N-monoalkyl diamine correspondingly.



Variation of molar quantity of H_2O combined with substituted diamines, with time. 1) N,N'-di-n-butylhexamethylenediamine, 2) N,N'-diisopropylhexamethylenediamine.

In order to direct the reaction towards the N-monosubstituent side, use was made of an observation made by us concerning the formation of solid, water-insoluble hydrates of both N-mono- and N,N'-dialkylated diamines.

It was established that in order to direct the reaction preferentially towards the N-monoalkylation side it should be carried out in an aqueous medium and the ratio of alkylating agent to diamine should be decreased (to 1 mole per mole of diamine). The increase in yield of monosubstituted diamine is fostered by the fact that in an aqueous medium it precipitates as a solid phase (in the form of the hydrate). This reduces the probability of the second amino group reacting with the alkylating agent and ensures that the reaction is directed mainly towards mono-alkylation.

The formation of hydrates was studied quantitatively from the example of disubstituted derivatives, namely N,N'-di-n-butyl- and N,N'-diisopropylhexamethylenediamine. Di-substituted diamines on addition of water, in an atmosphere saturated with water vapor, or on standing over water form, solid, crystalline, white hydrates. On placing these in a desiccator over P_2O_5 the water splits off completely and the residual diamine, by refractive index and nitrogen content, is identical with that first taken.

As is seen from the graph,* 1 mole of substituted diamine rapidly combines with 2 moles of H_2O to form the hydrate.** Further combination with water takes place much more slowly. Under the experimental conditions the maximum combination of water achieved was 4 moles per 1 mole of diamine. The dihydrate of N,N'-di-n-butylhexamethylenediamine is insoluble in water; the dihydrate of N,N'-diisopropylhexamethylenediamine dissolves in a large proportion of water. N,N'-diisobutyl-, N,N'-di-n-butyl-2-hexamethylenediamine, etc. also form hydrates.

* The data presented were calculated from the increase in weight of the diamine resulting from the addition of water in a desiccator over H_2O.

** Analysis of N,N'-di-n-butylhexamethylenediamine dihydrate. Found %: N (titrated) 10.5. M 280. $C_{14}H_{36}N_2O_2$. Calculated %: N 10.3. M 264.

Monosubstituted diamines (N-n-butyl- and N-isopropylhexamethylenediamine) also form crystalline hydrates in air (in an atmosphere saturated with H_2O vapor). For the monosubstituted diamines this fact was established qualitatively but was not studied quantitatively.

The formation of hydrates evidently explains the lowering of the yield of N,N'-dialkyl diamine and the formation of some quantity of N-monosubstituted diamine on carrying out the reduction alkylation reaction in water [1].

The method for preparing the monosubstituted derivative was worked out by us for N-mono-n-butylhexamethylenediamine but it can be used for the synthesis of other monosubstituted derivatives that form hydrates that are insoluble or difficultly soluble in water. N-monoisopropylhexamethylenediamine hydrate is soluble in a large proportion of water; however, even in this case carrying out the reaction in an aqueous medium increases the yield of the N-monosubstituted diamine. The results obtained are given in Table 1.

TABLE 1

Yield of N-Monoalkylhexamethylenediamine on Reduction Alkylation in Alcohol and in an Aqueous Medium

N-monosubstituted diamine	Whether hydrate is insoluble in water	Yield (in %) calculated on diamine taken	
		in alcohol	in water
N-Mono-n-butylhexamethylenediamine	+	20	65
N-Monoisopropylhexamethylenediamine	–	15	43

EXPERIMENTAL

Alkylation with n-butyraldehyde. A solution of 13.45 g hexamethylenediamine in 20 ml water was placed in an autoclave (volume 150-200 ml) and 8.3 g n-butyraldehyde and 0.2 g platinum oxide were added. The autoclave was closed, swept out with hydrogen and filled with hydrogen to 103 atmos and (at room temperature) placed on a shaker. Absorption of hydrogen was observed for a period of 40 min, the final pressure was 72 atmos corresponding to the absorption of 230 mmoles H_2 (100%). After completion of hydrogenation the crystals of the hydrate of the alkylated diamine were washed with 50 ml water on a vacuum filter. They were then dissolved in 100 ml ether, the solution dried with K_2CO_3 and after removal of catalyst and evaporation of the ether the residue was distilled in a current of nitrogen. The vapor temperature rose immediately to 101-102° (3 mm) and the first fraction corresponding to the N-monoalkyl derivative distilled within these limits. A jump in temperature to 130° (3 mm) was then observed, corresponding to distillation of the disubstituted derivative. There was little still residue. The yield of N-mono-n-butylhexamethylenediamine was 13.0 g (65% calculated on the diamine charge or 80% calculated on the diamine reacted). Analytical data are given in Table 2.

TABLE 2

Analysis of N-Monoalkyl Derivatives of Hexamethylenediamine

Substance	Boiling point (pressure in mm)	d_4^{25}	n_D^{25}	Analytical data (%) N (total) found (Kjeldahl)	N (total) calc.	N (amino) found (Van Slyke)	N (amino) calc.	Found Molecular wt. found	Found Molecular wt. calc.	MR_D found	MR_D calc.
N-Mono-n-butylhexamethylenediamine	101—102° (3)	0.833	1.4550	16.2	16.3	8.10	8.15	174	172	55.5	55.4
N-Monoisopropylhexamethylenediamine	87—87.5 (2)	0.830	1.4465	17.5	17.7	8.50	8.75	159	158	50.8	50.8

* Prepared and characterized for the first time.

Alkylation with acetone. 6.1 g acetone and 0.5 g platinum oxide were added to a solution of 12.2 g hexamethylenediamine in 25 ml water. A fall in hydrogen pressure from 107 to 79 atmos over a period of 30 min was observed, corresponding to 204 mmoles of absorbed hydrogen (97%). After completion of hydrogenation and settling of the catalyst the reaction mixture consisted of a homogeneous solution. In order to isolate the alkylation products the aqueous solution was extracted several times with ether. The ethereal layer was dried and the ether distilled off. On distilling the reaction products the vapor temperature rose immediately to 87-87.5° (2 mm) and the first fraction corresponding to the N-monoalkyl derivative was taken off within these limits. The temperature then rose to 104-106° (2 mm) at which temperature the second fraction was distilled off. The yield of N-monoisopropylhexamethylenediamine was 7.2 g (43% calculated on the diamine charge or 61% calculated on the diamine reacted). The analytical data are given in Table 2.

SUMMARY

1. A method has been developed for the synthesis of N-monoalkyl derivatives of hexamethylenediamine by reduction alkylation in an aqueous medium, characterized in that the product of monoalkylation separates in the hydrate form, which precipitates (for a number of carbonyl compounds) as a solid phase.

2. It has been established that also in cases where soluble hydrates are formed the use of water as solvent increases the yield of hexamethylenediamine N-monoalkyl derivatives.

3. Two hexamethylenediamine N-monoalkyl derivatives have been studied and characterized, N-monoisopropylhexamethylenediamine being synthesized for the first time.

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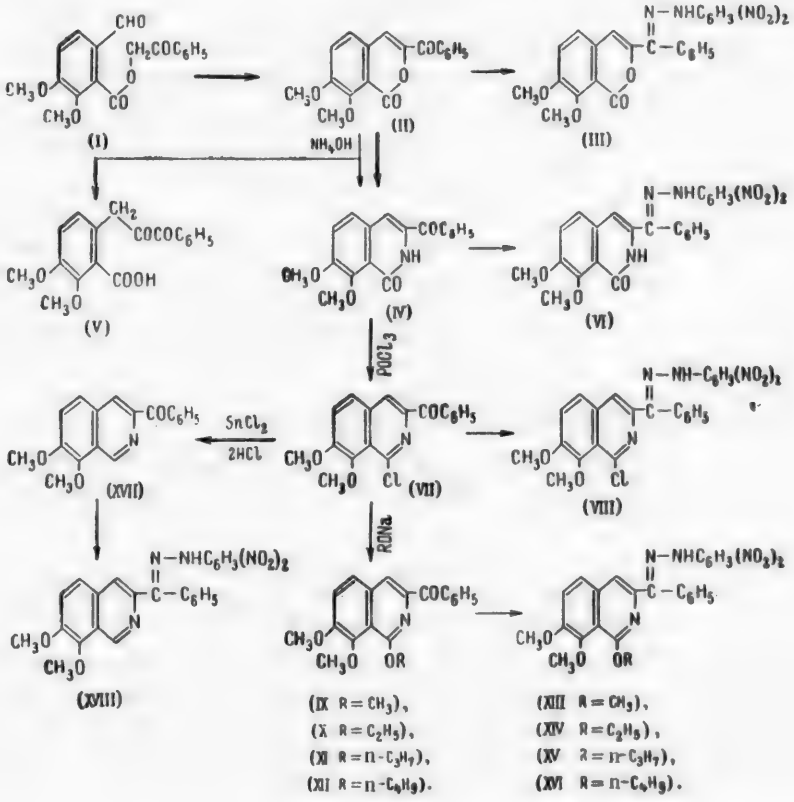
SYNTHESIS OF ALKOXY-SUBSTITUTED KETONES OF THE ISOQUINOLINE SERIES

L. I. Linevich

A large number of substances possessing high physiological activity and used in medicine are encountered among the isoquinoline compounds. A little studied group of isoquinoline compounds are the ketones of this series – substances which up to the present time are not readily available.

The problem of the present work consisted in the development of methods of preparation of a number of alkoxy-substituted ketones of the isoquinoline group from the available opianic (5,6-dimethoxy-o-aldehydobenzoic) acid, which occurs as a by-product in the production of the opium alkaloids. The ketones, the synthesis of which was developed, are close in structure to papaverine and papaveraldine – substances possessing spasmolytic activity. We achieved the synthesis of these ketones in a few stages as shown in the scheme below. (The thick arrows indicate the course of the main reaction.)



The preparation of the α-ester of opianic acid and ω-hydroxy acetophenone (I) from potassium opianate, and the preparation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (II) as a result of intramolecular condensation of this α-ester in the presence of piperidine has been reported earlier [1]. Further study of the conditions of intramolecular condensation of the above α-ester showed that on substitution of piperidine by diethylamine the yield is improved (60%). It was further shown that intramolecular condensation takes place also in the absence of a basic catalyst: on distilling the benzene from the filtrates obtained during crystallization of the α-ester the mixture was overheated; in this case not the original α-ester but (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (II), was found in the residue. This ketone was also obtained in high yield (90%) on distilling benzene from the pure α-ester on a sand bath. In the absence of benzene the ketone (II) is obtained from the α-ester only after more prolonged heating in vacuo at a higher temperature, considerable resinification occurring under these conditions. The ease with which the reaction proceeds on distilling off benzene is evidently explained by the fact that the benzene carries away the water formed in the condensation.

In order to characterize the ketone obtained, its 2,4-dinitrophenyl hydrazone (III) was prepared successfully. As has already been reported [1] this ketone does not react with a number of other carbonyl group reagents (hydroxylamine, semicarbazide) under the usual conditions.

Ketone (II) reacts with ammonia in acetic acid solution [1] forming (7,8-dimethoxyisocarbostyril -3)-phenyl ketone (IV). Further study of the amidation reaction, in particular amidation in an aqueous medium, showed that on heating a ketone of the isocoumarin series with aqueous ammonia hydrolysis of the isocoumaryl ring and formation of the diketo acid (V), previously described in the literature [2], takes place. This is the cause of the low (50%) yield of amidation product. In order to avoid hydrolysis of the starting material an attempt was made to carry out the reaction with aqueous ammonia in the cold. Amidation proceeds so slowly in the cold that it was practically impossible to detect any amidation product in the reaction mixture after 2-3 days and its quantitative formation was observed only after allowing the mixture to stand for 6 months.

For characterization of (7,8-dimethoxyisocarbostyril -3)-phenyl ketone (IV) its 2,4-dinitrophenyl hydrazone (VI) was prepared. The oxime and semicarbazone of this ketone could not be prepared either in alcohol or pyridine solution. This agrees with statements in the literature on the difficulty of preparing derivatives of some ketones of the isoquinoline series, the hetrocyclic nuclei of which are partially hydrolyzed [3].

Thus the study of the first three stages of synthesis of alkoxy-substituted ketones of the isoquinoline series led to the development of a method of preparation of (7,8-dimethoxyisocarbostyril- 3)-phenyl ketone (IV) with a total yield of about 80% of theory calculated on the initial potassium opianate.

Conversion of a ketone of the isocarbostyril series to 1-alkoxy-substituted ketones of the isoquinoline series could be achieved in two ways – either by direct alkylation of this derivative or by its conversion of a 1-chloro-substituted ketone of the isoquinoline series with subsequent substitution of the chlorine in the latter by alkoxy groups. On direct alkylation of isocarbostyril derivatives the possibility of forming O-alkyl and N-alkyl derivatives simultaneously is not excluded; consequently, we chose the second route. Hence, the next stage in the synthesis consisted in chlorination of (7,8-dimethoxyisocarbostyril -3)-phenyl ketone (VII). From this reaction (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (VI), not described in the literature, was obtained. For characterization of the ketone its 2,4-dinitrophenyl hydrazone (VIII) was prepared.

The optimum conditions for obtaining this ketone were found: on heating the parent ketone for a short time with phosphorus oxychloride it was obtained in quantitative yield. Carrying out the chlorination under other conditions (PCl_5, organic solvents) gave inferior results.

From the extensive data in the literature on the substitution of chlorine in heterocyclic nitrogen compounds, it is evident that chlorine in these compounds, in the α- and γ-positions relative to the nitrogen, generally exchanges with alkoxyl with sufficient ease on reacting with metal alcoholates.

On heating (1-chloro-7,8-dimethoxyisoquinoline-3)-phenyl ketone with sodium alcoholates in solution in the corresponding alcohol, a number of ketones, not previously known, were prepared: (1,7,8-trimethoxyisoquinolyl-3)-phenyl ketone (IX), (1-ethoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (X), (1-propoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XI), (1-butoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XII). The ketones were characterized by the 2,4-dinitrophenyl hydrazones (XIII-XVI).

In order to prepare a ketone of the isoquinoline series not containing an alkoxy group in position 1 in the isoquinoline nucleus, the 1-chloro-substituted isoquinoline ketone that we prepared was reduced. By using stannous chloride and hydrochloric acid as reducing agent (7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XVII), not previously known, was obtained. This ketone was characterized by the 2,4-dinitrophenyl hydrazone (XVIII).

EXPERIMENTAL

Preparation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (II). a) 3.28 g of the α-ester of opianic acid and ω-hydroxyacetophenone (I) were placed in a round-bottomed flask fitted with a reflux condenser and moistened with 10 drops of diethylamine. The mixture was heated on a boiling water bath. After heating for 16 hrs 10 ml ethyl alcohol and 10 ml toluene were added to the contents of the flask and heating was continued for a further 10-15 min. The mixture was then cooled and the crystals were filtered off and washed with alcohol. The crude product melted at 169-170°; after recrystallizing from ethyl alcohol m. p. 172°. According to the literature it has m. p. 172°. Yield 1.86 g, i. e., about 60%.

b) 3.28 g of the α-ester (I) and 10 ml benzene were placed in a round-bottomed flask fitted with a downward condenser and a thermometer reaching almost to the bottom of the flask. The benzene was distilled off from a sand bath; during this process the temperature of the mixture reached 160-170° and this temperature was maintained for 15-20 min. To the residue, consisting of a viscous, light-yellow liquid, 10 ml alcohol and 10 ml toluene were added. The mixture was cooled and the crystalline product was filtered off and washed with alcohol. M. p. 168°; after recrystallizing from alcohol and from toluene it remained unchanged. A test sample of the product mixed with (7,8-dimethoxyisocoumaryl-3)-phenyl ketone (m. p. 172°) melted at 170°. Yield 2.78 g (about 90%).

c) 3.28 g of the α-ester (I) was heated at 250-300° for 2 hrs in a round-bottomed flask connected to a vacuum pump. The reaction product was treated as in experiment "a". The crude product had m. p. 166-168°; after recrystallizing from alcohol, m. p. 168°. A sample mixed with (7,8-dimethoxyisocoumaryl-3)-phenyl ketone prepared in experiment "a" melted at 170°. Yield 1.91 g (about 70%).

(7,8-Dimethoxyisocoumaryl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (III). 0.5 g of 2,4-dinitrophenyl hydrazine was dissolved in 1 ml warm, concentrated sulfuric acid and 5 ml ethyl alcohol was added to the solution. Then a solution of 0.3 g ketone (II) in 50 ml ethyl alcohol was added immediately to the dinitrophenyl hydrazine solution. The 2,4-dinitrophenyl hydrazones obtained from preparations of ketone (II) formed under various conditions (experiments "a," "b" and "c") and also from the mixed test samples melted at the same temperature (m. p. 256° in a Maquenne block). Crystallization was carried out from a mixture of equal parts of alcohol and ethyl acetate.

Found %: N 11.60. $C_{24}H_{18}O_8N_4$. Calculated %: N 11.42.

Preparation of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone (IV). a) A mixture of 1.0 g ketone (II) and 100 ml of a 25% aqueous solution of ammonia was boiled for 3 hrs in a round-bottomed flask with a reflux condenser connected to a mercury trap. The mixture was then cooled and filtered and the residue washed with water. The residue consisted of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone. Yield 0.5 g (about 50%). M. p. 199° (from alcohol). Almost white crystals with a faint yellowish-green tinge. This substance was practically insoluble in water; readily soluble in dichloroethane, chloroform, pyridine and glacial acetic acid; slightly soluble in cold alcohol, soluble to a considerable extent on heating. Alcoholic solutions of ketone (IV) did not give the coloration with ferric chloride characteristic of the majority of isocarbostyril derivatives.

Found %: C 69.86; H 5.06; CH_3O 20.67; $H_{act.}$ 1.02. M 298. $C_{18}H_{15}O_4N$. Calculated %: C 69.89; H 4.89; $2CH_3O$ 20.07; $H_{act.}$ 1.00. M 309.

The filtrate from the separation of ketone (IV) from the reaction mixture was acidified with 10% sulfuric acid until acid to Congo. This brought about the separation of an acid which was filtered off and washed with water. Its melting point was 120-130° (decomp.). From its properties this acid was identical with the diketo acid obtained by Bain and co-workers [2] by alkaline hydroxlysis of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone. Yield 0.4 g (about 40%). For purification the acid was twice reprecipitated by water from solution in methyl alcohol. M. p. 128-130° (decomp.); according to the literature, m. p. about 130° (decomp.).

Found: neutralization equiv. 324. $C_{18}H_{16}O_6$. Calculated: neutralization equiv. 328.

b) A mixture of 0.5 g of finely powdered ketone (II) and 25 ml of 25% aqueous ammonia was allowed to stand at 8-10°. A sample of the solid material taken after 5 days had m. p. 172°; nitrogen could not be detected in the sample. No precipitate was obtained on acidifying the filtrate with sulfuric acid. The reaction mixture was left in a refrigerator and after 6 months the solid material was filtered off and washed with water. M. p. 199°. A mixed sample with ketone (IV) obtained previously [1] and in experiment "a" had m. p. 199°. Yield 0.45 g (quantitative, allowing for test sample removed). The filtrate obtained after separation of the solid product from the reaction mixture did not contain the diketo acid (V).

(7,8-Dimethoxyisocarbostyril-3)-phenyl ketone 2,4-dinitrophenylhydrazone (VI) was prepared by the method described above.

Found %: N 14.17. $C_{24}H_{19}O_7N_5$. Calculated %: N 14.31.

The 2,4-dinitrophenylhydrazone (VI) crystallized from glacial acetic acid with 1 molecule of acetic acid.

Preparation of (1-chloro-7,8-dimethoxyisoquinoline-3)-phenyl ketone (VII). 3.1 g of ketone (IV) and 3 ml (excess) phosphorus oxychloride were placed in a round-bottomed flask fitted with a reflux condenser and a calcium chloride drying tube. The mixture was heated on a boiling water bath for 20 min, then after cooling, poured onto ice. The product, which crystallized out rapidly, was filtered off and washed with water. The yield of ketone (VII)was 3.1 g(99%) with m. p. 144° (from benzene or ethyl alcohol). Ketone (VII) was a colorless, crystalline substance. It was practically insoluble in water but soluble in organic solvents.

Found %: C 66.08; H 4.48; N 4.30; Cl 10.80. $C_{18}H_{14}O_3NCl$. Calculated %: C 65.96; H 4.31; N 4.27; Cl 10.82.

(1-Chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (VIII) was prepared by the method described above. The orange crystals of the dinitrophenylhydrazone were filtered off after 10 min (to avoid hydrolysis with splitting off of chlorine in the acidic medium). M. p. (in a Maquenne block) 236-242° (from nitrobenzene).

Found %: 13.87. $C_{24}H_{18}O_6N_5Cl$. Calculated %: N 13.79.

Preparation of the (1-alkoxy-7,8-dimethoxyisoquinoline-3)-phenyl ketones (IX-XII). To a solution of 3.28 g of ketone (VII) in 150 ml of the alcohol (methyl, ethyl, propyl, butyl) a solution of the sodium alcoholate, prepared from 0.25 g sodium and 10 ml of the same alcohol, was added. The mixture was heated on the water bath at 60-70° for 16 hrs, the reflux condenser being connected to a calcium chloride tube. The sodium methylate, ethylate and propylate reaction products were isolated by pouring the reaction mixtures into 300 g ice-water. The product which separated was filtered off, washed with water to neutral reaction to phenolphthalein and recrystallized from ethyl alcohol. To isolate the sodium butylate reaction product the mixture was washed with water to neutral reaction to phenolphthalein, the solution of the ketone in butyl alcohol dried over sodium sulfate and the alcohol distilled off in vacuo.

a) (1,7,8-Trimethoxyisoquinolyl-3)-phenyl ketone (IX). Yield 2.74 g (85%); m. p. 134°.

Found %: C 70.65; H 5.43; N 4.39. $C_{19}H_{17}O_4N$. Calculated %: C 70.58; H 5.30; N 4.33.

b) (1-Ethoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (X). Yield 2.66 g (79%); m. p. 120°.

Found %: C 71.16; H 5.85; N 4.15. $C_{20}H_{19}O_4N$. Calculated %: C 71.20; H 5.68; N 4.15.

c) (1-Propoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XI). Yield 2.88 g (82%); m. p. 78°.

Found %: C 71.81; H 6.02; N 4.02. $C_{21}H_{21}O_4N$. Calculated %: C 72.31; H 6.34; N 3.83.

d) (1-Butoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XII). Yield 3.06 g (84%); m. p. 91-92° (from alcohol.

Found %: C 72.42; H 6.27; N 3.97. $C_{22}H_{23}O_4N$. Calculated %: C 72.31; H 6.34; N 3.83.

The ketones obtained were crystalline solids, practically insoluble in water, soluble in organic solvents. On passing dry hydrogen chloride through ethereal solutions of the ketones the corresponding salts, which are readily hydrolyzed by water, separated out.

The 2,4-dinitrophenylhydrazones of these ketones were prepared by the method described above. These derivatives were recrystallized from a mixture of equal volumes of alcohol and ethyl acetate.

a) (1,7,8-Trimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XIII). M. p. 174-175°.

Found %: N 14.16. $C_{25}H_{21}O_7N_5$. Calculated %: N 13.91.

b) (1-Ethoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XIV). M. p. 210°.

Found %: N 13.64. $C_{26}H_{23}O_7N_5$. Calculated %: N 13.50.

c) (1-Propoxy-7,8-dimethoxyisoquinonyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XV). M. p. 178°

Found %: N 13.28. $C_{27}H_{25}O_7N_5$. Calculated %: N 13.19.

d) (1-Butoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XVI). M. p. 137-138°.

Found %: N 12.49. $C_{28}H_{27}O_7N_5$. Calculated %: N 12.84.

Preparation of (7,8-dimethoxyisoquinolyl-3)-phenyl ketone (XVII). A mixture of 3.28 g (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone (VII), 2.48 g of finely powdered $SnCl_2 \cdot 2H_2O$ and 12 ml conc. HCl (d 1.18) was heated on a wire gauze under reflux for half an hour. The solid material rapidly dissolved and after 15-20 min a crystalline product began to separate. Heating was continued for a further 3 hrs (on a boiling water bath) after which the reaction mixture was cooled to room temperature and the crystals filtered off and washed with concentrated hydrochloric acid. The crystalline product was heated with 50 ml 10% KOH for half an hour, after which the mixture was cooled and filtered. The solid product was washed with KOH solution and water, dried and extracted with ether. The ether was distilled from the ethereal extract and the residue, consisting of ketone (XVII), was recrystallized from petroleum ether and from alcohol. Yield 1.03 g (35%).

M. p. 104°. This material was slightly soluble in water, readily soluble in ether and the majority of organic solvents.

Found %: C 73.71; H 5.20; N 4.72. $C_{18}H_{15}O_3N$. Calculated %: C 73.71; H 5.16; N 4.77.

The residue after extraction of ketone (XVII) with ether was extracted several times with hot chloroform. The residue (1.4 g) after removal of chloroform was a crystalline substance with m. p. 238° (from nitrobenzene), practically insolubie in water and in ether; in the majority of organic solvents it was only slightly soluble in the cold.

(7,8-Dimethoxyisoquinolyl-3)-phenyl ketone 2,4-dinitrophenylhydrazone (XVIII) was prepared by the method described above. M. p. 268° (from nitrobenzene in a Maquenne block).

Found %: N 12.04. $C_{24}H_{13}O_6N_5 \cdot H_2SO_4$. Calculated %: N 12.25.

SUMMARY

A method has been developed for the preparation from opianic acid of a number of alkoxy-substituted ketones of the isoquinoline group. The preparation of these ketones was accomplished in a few stages as follows:

1. Intramolecular condensation of the α-ester of opianic acid and ω-hydroxyacetophenone. It was shown that this reaction takes place both with and without organic bases. Conditions have been found for the preparation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone in high yield (90%).

2. Amidation of (7,8-dimethoxyisocoumaryl-3)-phenyl ketone. It was shown that amidation in glacial acetic acid proceeds more satisfactorily than in aqueous solution.

3. Chlorination of (7,8-dimethoxyisocarbostyril-3)-phenyl ketone. Conditions were found whereby (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone could be prepared in quantitative yield.

4. a) Reaction of (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone with sodium alcoholates whereby a number of (1-alkoxy-7,8-dimethoxyisoquinolyl-3)-phenyl ketones were obtained, with different alkoxy groups (OCH_3, OC_2H_5, OC_3H_7, OC_4H_9) in position 1.

b) Reduction of (1-chloro-7,8-dimethoxyisoquinolyl-3)-phenyl ketone with stannous chloride and hydrochloric acid, giving (7,8-dimethoxyisoquinolyl-3)-phenyl ketone.

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THE ACTION OF NITROUS ACID ON CYCLIC SALTS OF SALICYLIC ACID. THE PREPARATION OF 5-DIAZOSALICYLIC ACID

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V. M. Rodionov and V. K. Matveev [1] have shown that 5-diazo-2-phenolsulfonic acid and 3-diazo-4-phenolsulfonic acid are formed readily by the action of nitrous acid on o- and p-phenolsulfonic acids. The formation of the diazo compounds in this way proceeds through the stage of the corresponding nitroso compounds which by reacting further with oxides of nitrogen and nitrous acids are converted to the diazonium nitrates [2, 3].

In the case of salicylic acid the preparation of the corresponding nitroso compound by the action of nitrous acid has not so far been successful. Salicylic acid is evidently not sufficiently reactive for this. Papers describing the preparation of nitrososalicylic acid by the action of nitrous acid [4, 5] were shown to be in error [6]. Salicylic acid in this case reacts with nitrous acid with evolution of CO_2 and the formation of o-diazophenol. o-Nitrosophenol is formed as an intermediate product.

Study of the reactivity of cyclic salts of salicylic acid with respect to azo coupling indicates that some of these have a considerably increased reactivity in this reaction, in comparison with free salicylic acid. Cyclic aluminum, chromium, zinc and beryllium salicylates were shown to be particularly active under conditions where intramolecular dissociation [7], which for the cyclic salicylates mentioned takes place in acidic media, occurred to a sufficient extent. For this reason the cyclic salicylates in acid media have the same activity as that of alkaline solutions of salicylic acid having the same degree of dissociation of the phenolic hydroxyl.

Since the azo coupling reaction of phenols and naphthols is very similar to the nitrosation reaction [8, 9] an increase in the activity of the above-mentioned cyclic salicylates in the nitrosation reaction, might also be expected. In confirmation of this assumption it was established that the cyclic salicylates have a high reactivity in the reaction in question and react with nitrous acid with the addition of a nitroso group in the para position relative to the hydroxyl. The carboxyl group in the cyclic salicylates, in contrast to that in free salicylic acid, does not split off under these conditions. The complex-forming element, in addition to increasing the reactivity in the nitrosation reaction, by virtue of its positive charge prevents the transfer of the free electron pair from the carboxyl oxygen to the nucleus, and splitting off of CO_2. This second function of the complex-forming element can also be achieved by a proton, which results in a greater stability in the bond between the carboxyl group and the aromatic nucleus in a strongly acidic medium. Consequently, on reacting salicylic acid with nitrous acid in a medium of concentrated sulfuric acid, 3-nitrosalicylic acid or 5-nitrosalicylic acid are formed, depending on the reaction conditions [10]. In spite of the rigorous reaction conditions only an insignificant proportion of the salicylic acid reacts with splitting off of CO_2.

Although increasing the hydrogen ion concentration also leads to greater stability of the bond between the carboxyl group and the nucleus, in view of the depression of dissociation of the phenolic hydroxyl, salicylic acid has a considerably lower activity under these conditions in comparison with its intramolecularly ionized cyclic salts.

The cyclic salt of 5-nitrosalicylic acid formed, reacts further with nitrous acids to form the corresponding salt of 5-diazosalicylic acid. In this connection the composition of the reaction product varies with changes in the amount of nitrous acid introduced: with equimolecular proportions of salicylic and nitrous acids the nitroso compound is formed in 60-70% yield and the diazo compound in 10-12% yield depending on the cyclic salt taken; furthermore 20-28% of the salicylic acid remains unchanged. Increasing the amount of nitrous acid to 5.5 moles per 1 mole of salicylic acid results in the formation of only 5-diazosalicylic acid in over 90% yield.

EXPERIMENTAL

Reaction between cyclic aluminum salicylate and nitrous acid. To 8.0 g (0.050 g-mole) sodium salicylate dissolved in 50 ml water 14.5 g (0.060 g-mole) $AlCl_3 \cdot 6H_2O$ in 100 ml water was added. The pH of the solution was found before mixing to be 8.0 and 3.2, respectively; as a result of complex formation the pH of the mixture fell to 2.7. To the mixture obtained a solution of 3.8 g (0.055 g-mole) of sodium nitrite in 25 ml water was added and the resulting mixture was allowed to stand in the dark for 24 hrs at 20°. A 10% solution of hydrochloric acid was then added to give a faint reaction to Congo. Nitrous acid was not detected. The solution was transferred to a 500 ml measuring flask and made up to the mark with water.

The presence of the nitroso compound among the reaction products was confirmed by a qualitative test carried out according to [11]. Also the formation of azo compounds by azo coupling with alkaline solutions of resorcinol and 1,8-aminonaphthol-3,6-disulfonic acid indicated the presence of the diazo compound (11.2% calculated on the salicylic acid). The diazo compound was determined by the quantity of nitrogen evolved on boiling an aliquot portion of the solution with a cuprous chloride solution acidified with hydrochloric acid [12].

For determination of the nitroso compound content 0.25 g resorcinol dissolved in 25 ml of 10% sodium carbonate solution was added to 25 ml of the above solution and the azo compound formed was titrated with a vanadous sulfate solution [13]. The nitroso compound content, determined from the difference between the total azo and nitroso compound content and that of the diazo compound, was 63.8%.

If after the addition of 3.8 g of sodium nitrite to the reaction mixture the addition of $NaNO_2$ is continued so as to give a total quantity of 19.0 g (0.275 g-mole) over a period of 8-10 hrs, with simultaneous addition of concentrated hydrochloric acid to maintain a faint reaction to Congo, then only 5-diazosalicylic acid is formed. Its yield, determined by the same method [12] after removal of excess nitrous acid by the addition of sulfaminic acid, was 90.8%. Evaporation of an aliquot part of the reaction mixture in vacuo and acidification of the dry residue with 10% hydrochloric acid yielded 5-diazosalicylic acid, identified by the absorption spectra of the azo compounds formed with resorcinol and 1,8-aminonaphthol-3,6-disulfonic acid.

For determination of the amount of CO_2 evolved the reaction mixture was connected to a potash bulb and the gases evolved were absorbed in KOH solution. The absence of CO_2 in the absorbed gases was confirmed by a negative reaction with $Ba(OH)_2$.

Reaction between cyclic zinc salicylate and nitrous acid. When in the previous example 17.0 g (0.050 g-mole) zinc chloride was taken in place of aluminum chloride the quantities of diazo and nitroso compounds formed were 11.8% and 60.8%, respectively. On increasing the quantity of $NaNO_2$ to 19.0 g (0.275 g-mole) the nitroso compound was absent from the reaction mixture. The yield of diazo compound was 90.5%. The diazo compound was isolated and identified as 5-diazosalicylic acid in the same manner as in the previous example.

Reaction of cyclic chromium salicylate with nitrous acid. To 8.0 g (0.050 g-mole) sodium salicylate dissolved in 50 ml of hot water 50 ml of a solution containing 16 g $CrCl_3 \cdot 6H_2O$ was added and 25 ml of 10% sodium carbonate solution was then added with stirring. The mixture was then heated to boiling and refluxed for 1 hr. 75 ml of water was next added, the mixture cooled to 20° and further treated as in the previous examples. The addition of 3.8 g (0.055 g-mole) sodium nitrite yielded 69.4% of 5-nitrososalicylic acid and 9.8% of 5-diazosalicylic acid. On increasing the quantity of added sodium nitrite to 19.0 g (0.275 g-mole) with simultaneous addition of concentrated hydrochloric acid to maintain a faint reaction to Congo, only 5-diazosalicylic acid was formed in 92.6% yield.

SUMMARY

Cyclic salts of salicylic acid under conditions favoring their intramolecular dissociation possess high activities in the nitrosation reaction in comparison with salicylic acid. At the same time the complex formation suppresses the splitting off of CO_2, which occurs when salicylic acid reacts with nitrous acid.

It is shown that by the interaction of cyclic salts of salicylic acid with equimolar quantities of nitrous acid 5-nitrososalicylic acid is formed in 60-70% yield together with a small quantity of 5-diazosalicylic acid (10-12%). Increasing the quantity of nitrous acid to 5 moles leads to the formation of only 5-diazosalicylic acid in 90-93% yield.

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DIMETHYL ARYLSULFON-N-METHYLAMIDOPHOSPHATES

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A large number of diesters of arylsulfonamidophosphoric acids have recently been prepared [1]. It is assumed, though not proved, that they have the amide structure (I). However, the possibility is not excluded that compounds of type (I) exist in equilibrium with the phosphazo form (II).

$$\underset{\text{(I)}}{ArSO_2NH{-}PO(OR)_2} \rightleftarrows \underset{\text{(II)}}{ArSO_2N{=}P(OR)_2(OH)}$$

To decide the question of the structure of diesters of arylsulfonamidophosphoric acids by chemical means is scarcely possible and for elucidation of their structure by physical means it is necessary to have, as reference samples, substances known to have structures (I) and (II). Many substances of structure (II) are known [1, 2] but there are no compounds authentically known to have structure (I). It was therefore of interest to carry out alkylation of the silver and sodium salts of diesters of arylsulfonamidophosphoric acids. By this means it would be possible to decide whether phosphazo compounds or esters of N-alkylated arylsulfonamidophosphoric acids are produced, since cases are known where alkylation of silver and sodium salts takes place in one case on the nitrogen and in the other case on the oxygen atom.

With this objective we investigated the methylation of silver and sodium salts of dimethyl arylsulfonamidophosphates. The sodium salts could not be methylated successfully. On prolonged heating with methyl iodide on a boiling water bath the sodium salts remained unchanged and with dimethyl sulfate they formed substances with unpleasant odors. The silver salts, on the other hand, reacted readily with methyl iodide forming dimethyl arylsulfon-N-methylamidophosphates.

$$ArSO_2NAg{-}PO(OCH_3)_2 + CH_3I \longrightarrow AgI + ArSO_2N(CH_3){-}PO(OCH_3)_2$$

By this means the N-methyl derivatives of dimethyl arylsulfonamidophosphates were prepared.

$$ArSO_2N(CH_3){-}PO(OCH_3)_2,$$

where Ar = o-$CH_3C_6H_4$, α-$C_{10}H_7$, β-$C_{10}H_7$.

All of these are neutral materials, insoluble in alkalis. On prolonged boiling with aqueous-alcoholic hydrochloric acid solution they are hydrolyzed to N-methylarylsulfonamides, which indicates their structure.

$$ArSO_2N(CH_3){-}PO(OCH_3)_2 + H_2O \xrightarrow{H^+} ArSO_2NHCH_3$$

The N-metnyl derivatives dissolve readily in methyl iodide, acetone, benzene and hot alcohol, with difficulty in petroleum ether and are insoluble in water.

The dimethyl esters of α- and β-naphthylsulfon-N-methylamidophosphoric acids are crystalline materials with melting points of 91 and 82°, respectively. The melting points of the isomeric trimethyl esters are 84-85° and 93-94°, respectively [1].

Dimethyl o-tolylsulfon-N-methylamidophosphate was not obtained in the pure state: the reaction product could not be distilled without decomposition to a viscous, oily liquid.

EXPERIMENTAL

Preparation of the silver salts of the dimethyl arylsulfonamidophosphates. To a solution of 0.01 g-mole of the sodium salt of the dimethyl arylsulfonamidophosphate in 10-20 ml water an equimolar quantity of silver nitrate was added and the solution was allowed to stand overnight. The crystalline silver salt that separated was isolated and crystallized from water or alcohol. All operations of separation and purification were necessarily carried out in artificial light.

α-$C_{10}H_7SO_2NAg-PO(OCH_3)_2$. Yield 3.71 g (87.9%). Large prisms (from alcohol), dissolving easily in hot water, with difficulty in cold water and in alcohol; m. p. 155-157°.

Found %: Ag 25.39; OCH_3 14.47. $C_{12}H_{13}O_5NSPAg$. Calculated %: Ag 25.26; OCH_3 14.71.

β-$C_{10}H_7SO_2NAg-PO(OCH_3)_2$. Yield 4.18 g (99.1%). Small prisms (from water), m. p. 159-160°.

Found %: OCH_3 14.35. $C_{12}H_{13}O_5NSPAg$. Calculated %: OCH_3 14.71.

o-$CH_3C_6H_4SO_2NAg-PO(OCH_3)_2$. Yield 3.38 g (87.5%). The salt dissolved comparatively easily in cold water, very easily in hot water. Decomposes readily (particularly in a moist condition) in sunlight; m. p. 182-183°.

Preparation of the dimethyl N-methylamidophosphates. 0.02 g-mole of the silver salt and 20 ml methyl iodide were refluxed for 5-6 hrs. Silver iodide and the unreacted silver salt were filtered off and the filtrate evaporated. The oily liquid obtained in the case of the α- and β-naphthyl derivatives gradually crystallized out.

Dimethyl α-naphthylsulfon-N-methylamidophosphate. Yield of crude product 6.27 g (95.2%). Long prisms (from carbon tetrachloride) with m. p. 91°.

Found %: OCH_3 18.81, 18.91. $C_{13}H_{16}O_5NSP$. Calculated %: OCH_3 18.85.

Dimethyl β-naphthylsulfon-N-methylamidophosphate. Yield 4.42 g (67.0%). Long, thin, lustrous needles (from petroleum ether) with m. p. 82°.

Found %: OCH_3 18.90. $C_{13}H_{16}O_5NSP$. Calculated %: OCH_3 18.85.

Dimethyl o-tolylsulfon-N-methylamidophosphate. Yield 2.30 g (78.5%). Viscous oil, decomposes on distillation. Freed from a considerable amount of impurities by treatment with boiling petroleum ether.

Found %: OCH_3 20.65. $C_{10}H_{16}O_5NSP$. Calculated %: OCH_3 21.18.

Hydrolysis of dimethyl α-naphthylsulfon-N-methylamidophosphate. 0.822 g of the dimethyl ester, 10 ml alcohol and 10 ml 2N hydrochloric acid were refluxed for 20 hrs. The hot mixture was freed from a small quantity of oily droplets and left to crystallize for 24 hrs. Yield of N-methyl-α-naphthalenesulfonamide 0.35 g (63.3%). The melting point of 136° agrees with that in the literature [3].

SUMMARY

Dimethyl arylsulfon-N-methylamidophosphates, isomeric with the trimethoxyphosphazosulfonaryls, have been synthesized.

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Dnepropetrovsk Metallurgical Institute

• Original Russian pagination. See C. B. translation.

ALKALOIDS OF PEGANUM HARMALA L.

II. THE STRUCTURE OF TWO NEW ALKALOIDS

N. I. Koretskaia and L. M. Utkin

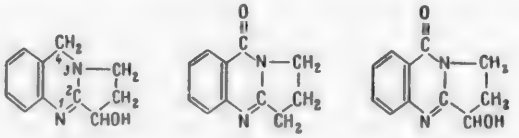
The isolation of peganine (I), harmine and two new bases designated as alkaloid No. 1 ($C_{11}H_{10}ON_2$) and alkaloid No. 2 ($C_{11}H_{10}O_2N_2$) from the parts of the rue (peganum harmala L.) growing above ground, has been reported earlier [1].

Continuing the investigation of the structure of the newly isolated substances reported in that communication we have found that on reduction of alkaloid No. 1 with lithium aluminum hydride dihydrodesoxypeganine ($C_{11}H_{14}N_2$) [2, 3] is formed. The occurrence of a bond at 1675 cm^{-1} (amide carbonyl) in the infrared absorption spectrum of alkaloid No. 1 enables the assumption to be made that it is an oxo derivative of desoxypeganine [2, 4]. According to its constants and elementary analysis alkaloid No. 1 is identical with 2,3-trimethylele-quinazolone-4 (II), which is described in the literature [4]. The identity of these substances was shown by a direct comparison of the two.

The infrared absorption spectrum of alkaloid No. 2 shows that this substance contains an hydroxyl group in addition to carbonyl amide. This suggests that alkaloid No. 2 is an oxo derivative of peganine, namely L-2,3-(α-hydroxytrimethylene)-quinazolone-4 (III). The racemate of this material, obtained by the oxidation of DL-peganine with hydrogen peroxide, has been described in the literature [4, 5]. L-2,3-(α-hydroxytrimethylene)-quinazolone-4, which we synthesized from L-peganine by the same method, was identical with alkaloid No. 2.

Thus, we have shown that the parts of the rue (Peganum harmala L.) growing above ground contain, in addition to peganine, substances that are either products of its decomposition or its precursors in the process of this alkaloid in the plant. The solution of the problem of the role which these substances play in the processes of transformation of peganine could probably be found by a study of the relationship of all three 2,3-trimethylene-quinazoline derivatives in the various stages of vegetation of the plant.

It is interesting to note that by reduction of 2,3-(α-hydroxytrimethylene)-quinazolone-4 with zinc in dilute hydrochloric acid, 2,3-trimethylenequinazolone-4 and desoxypeganine were obtained.



(I) (II) (III)

EXPERIMENTAL

Reduction of alkaloid No. 1 with lithium aluminum hydride. 2 g alkaloid No. 1 and 1 g $LiAlH_4$ in 150 ml anhydrous ether were refluxed for 7 hrs. Excess $LiAlH_4$ was decomposed by the addition of 3 ml water and 40 ml of a 10% solution of NaOH and 25 ml of a saturated solution of Seignette's salt (potassium sodium tartrate). The ether layer was separated and the alkaline suspension was exhaustively extracted with ether. After evaporation of the dried ethereal solution 1.53 g of material was obtained. Recrystallization from petroleum ether removed 0.3 g of unchanged alkaloid No. 1. The mother liquor was evaporated in vacuo; from the residue (0.95 g) a sub-

stance with m. p. 69-70° was obtained after repeated recrystallization from ether; R_f 0.51 (system I*, developer – Dragendorff's reagent) and 0.32 (system II, developer as above).

Found %: C 75.85; H 7.99; N 16.07. $C_{11}H_{14}N_2$. Calculated %: C 75.82; H 8.10; N 16.08.

Admixture with dihydrodesoxypeganine, prepared by reduction of peganine with sodium in amyl alcohol [3], gave no depression of the melting point.

Oxidation of L-peganine to L-2,3-(α-hydroxytrimethylene)-quinazolone-4 by hydrogen peroxide. 1 g L-peganine, 13 ml acetone and 10 ml 30% H_2O_2 were heated for 2 hrs at 55°. The solution was evaporated in vacuo to 5 ml, made alkaline with ammonia and extracted with chloroform. The residue after distilling off the chloroform was treated with 5 ml anhydrous ether and the solid residue (0.62 g) filtered off. After recrystallization from methanol the product had m. p. 202-203°; $[\alpha]^{18}D$ 128.9° (c 0.7; $CHCl_3$); R_f 0.70 (system II, developer – a solution containing 1% $KMnO_4$ and 1% Na_2CO_3).

Found %: C 65.54; H 4.85; N 13.61. $C_{11}H_{10}O_2N_2$. Calculated %: C 65.33; H 4.98; N 13.85.

No depression of the melting point was observed on mixing with alkaloid No. 2. The infrared spectra of the two materials coincided.

Reduction of alkaloid No. 2 with zinc dust in hydrochloric acid. A solution of 3.0 g alkaloid No. 2 in 100 ml 10% HCl was stirred with 10 g zinc dust for 8 hrs (20°). Excess zinc was filtered off and washed with water. The filtrate was made alkaline with ammonia and extracted with chloroform. The chloroform extract was evaporated to 50 ml and passed through a column containing 100 g Al_2O_3. On washing out with chloroform 1.05 g of a semicrystalline material was isolated, giving 0.67 g of a crystalline hydrochloride of m. p. 250-251° (from methanol) by treatment with an alcoholic HCl solution. The base obtained from the hydrochloride in the usual way had m. p. 109.5-110.5 (from petroleum ether), R_f 0.83 (system II, developer – Dragendorff's reagent).

Found %: C 71.26; H 5.49. $C_{11}H_{10}ON_2$. Calculated %: C 70.95; H 5.41.

The mixed melting point with 2,3-trimethylenequinazolone-4, prepared by oxidation of desoxypeganine with hydrogen peroxide [4], was 109.5-110.5°.

The filtrate after separation of the crystalline hydrochloride was diluted with anhydrous ether. The residue (0.27 g) which precipitated was purified by repeated solution in alcohol and precipitation with ether. This material then had m. p. 254°.

Found %: Cl 16.97. $C_{11}H_{12}N_2 \cdot HCl$. Calculated %: Cl 16.99.

A base with m. p. 87-88° (from ether) was obtained from the hydrochloride, R_f 0.19 (system II, developer – Dragendorff's reagent); a mixed melting point with desoxypeganine [4] gave no depression.

SUMMARY

Alkaloids No. 1 and No. 2 isolated previously from the parts of Peganum harmala L. growing above ground are identical with 2,3-trimethylenequinazolone-4 and L-2,3-(α-hydroxytrimethylene)-quinazolone-4, respectively. The presence of these compounds in a plant has been established for the first time.

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* See comunication I [1] for the composition of the solvents (system I and system II).

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INVESTIGATIONS IN THE FIELD OF INDOLE DERIVATIVES*

V. THE PROBLEM OF THE MECHANISM OF THE FISCHER REACTION

N. N. Suvorov, N. P. Sorokina, and Iu. N. Sheinker

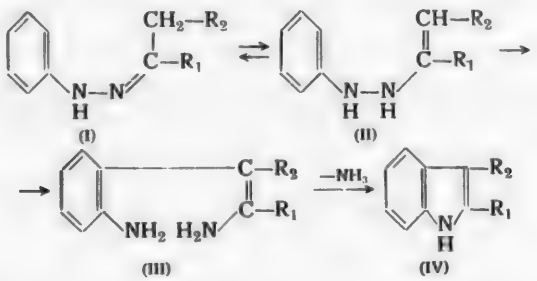
The conversion of arylhydrazones of carbonyl compounds to indole derivatives (the Fischer reaction) is an important and the most general method of preparing the latter. There are two methods of carrying out this reaction; the first of these, due to Fischer [2] proposes the use of condensing media of an acidic nature (mineral acids, anhydrous zinc chloride, boron trifluoride, etc.) in a quantity of at least 1 mole per mole of arylhydrazone, but in practice needing a large excess; the second is the method of A. E. Arbuzov [3]— comprising catalytic decomposition of the arylhydrazones. In both cases the formation of the indole derivative is accomplished by the separation of a molecule of ammonia (in the case of the Fischer method in the form of an ammonium salt) from the arylhydrazone molecule resulting from a preliminary intramolecular rearrangement in the latter.

Sound views on the mechanism of this interesting reaction were first developed by Brunner [4], whose work has remained completely unnoticed. The modern treatment of the mechanism of this reaction is connected in the chemical literature with the names of G. and R. Robinson who proposed in 1918, independently of Brunner, an analogous scheme, basing it on a number of indirect considerations [5]. The English investigators consider that the conversion of an arylhydrazone to an indole derivative consists of 3 stages:

1) tautomeric conversion of the arylhydrazone (I) to the corresponding unsaturated hydrazine (II),

2) ortho-benzidine rearrangement of the hydrazo compound (II) to the unsaturated diamine (III),

3) formation of the indole ring (IV) resulting from the elimination of a molecule of ammonia.



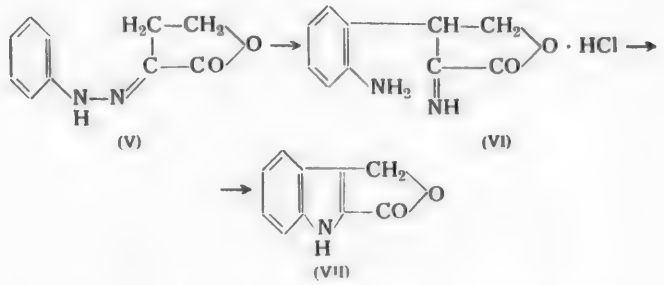
It should be mentioned that a number of other explanations of the Fischer reaction have been suggested [6-9]; however, they are inconsistent with the experimental facts and will not be considered here.

The most conclusive confirmation of the Robinson scheme is given by investigations carried out with the help of phenylhydrazine with "labeled" nitrogen N^{15} [10, 11]: this scheme requires for the formation of N-substituted indoles, readily obtained by the Fischer reaction from assymmetric alkyl (aryl) phenylhydrazones, the

* For previous communications in this series see [1]. The present paper was read at the meeting of the Section of Organic Chemistry of the Moscow Section of the D. I. Mendeleev All-Union Chemical Society on March 11, 1957.

elimination of the nitrogen atom furthest away from the benzene nucleus, which was also established by means of labeled nitrogen. However, there is no direct evidence based on isolation of the two intermediate products (the unsaturated hydrazine (II) and the diamine (III)). For this reason attempts have been made, though not on a sufficiently sound basis, to cast doubt on the mechanism of the Fischer reaction suggested by G. and R. Robinson [12].

Only one example is known of the isolation of an intermediate product in a Fischer reaction. In 1950 Plieninger by passing gaseous hydrogen chloride into a solution of α-keto-γ-butyrolactone phenylhydrazone (V) in galcial acetic acid succeeded in obtaining a compound to which the structure α-imino-β-(2-aminophenyl)-γ-butyrolactone hydrochloride (VI) was ascribed [13]. Later it was shown that (VI) on heating with hydrochloric acid gives the corresponding indole derivative (VII) [14].



(V) (VI) (VII)

It should be noted however that the structure of compound (VI) was not definitely proved since for this purpose a reaction was used (acetylation with acetic anhydride in pyridine), which does not exclude the possibility of isomerization.

We felt that by carrying out the Fischer reaction in acetic anhydride it should be possible to detect the intermediate product in the acetylated form and thus to obtain direct evidence of the correctness of G. and R. Robinson's scheme. Methylethyl ketone phenylhydrazone, which very readily and in excellent yield gives 2,3-dimethylindole under the conditions of the Fischer reaction, was chosen as the material for investigation. Having the objective of isolating the acetylated intermediate product we decided to carry out the reaction under the conditions normally used for the preparation of enol acetates of ketones, since there is a definite parallelism between the formation of the unsaturated hydrazo compound (II) and the enolization of carbonyl compounds, as was noted at the time by the Robinsons. On refluxing methylethyl ketone phenylhydrazone (VIII) with acetic anhydride in the presence of catalytic quantities of p-toluenesulfonic acid (or with an equimolar quantity in the cold) a crystalline substance, with the composition $C_{14}H_{18}O_2N_2$ and m. p. 57-58°, is formed in 87% yield. This substance contains two acetyl groups, one double bond (shown by catalytic hydrogenation and by bromine addition) and contains no active hydrogen. On boiling for a short time with dilute mineral acids it gives 2,3-dimethylindole and can therefore be regarded as an intermediate product in the formation of the latter. 2,3-Dimethylindole is formed also by distilling this diacetyl derivative with zinc dust. The data obtained enable the structure 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 (IX) or the isomeric 2-acetylamino-3-(o-acetylaminophenyl)-butene-2 (X) to be assigned to the compound $C_{14}H_{18}O_2N_2$. In order to choose between these two structures the infrared spectrum of this compound was examined. In the infrared spectrum (Fig. 1) there is no absorption band in the region 3000-3400 cm^{-1} indicating the absence of an N—H bond from the compound. In the region characteristic of double bonds there are two almost coincident, intensive bands at 1690 and 1664 cm^{-1} corresponding to the two amide carbonyl groups C=O, evidently differing somewhat because of their position in the molecule. Again at 1592 cm^{-1} there is a band of low intensity caused by the aromatic system of double bonds of the benzene nucleus. The absence from the spectrum of the band characteristic of the N—H bond (3000-3400 cm^{-1}) eliminates structure (X) for the compound in question, which differs from the other by the presence of two N—H bonds in the molecule.

Definite evidence for the structure of the compound with m. p. 57-58° was obtained by a study of its catalytic hydrogenation. An attempt to rupture the N—N bond presumed to be present was unsuccessful: on hydrogenation in an autoclave at 42 atmos and 60° for a period of 7 hrs in the presence of a very large quantity of Raney nickel (W-4) reduction of only the double bonds occurred and it was not possible to find even a trace of aniline

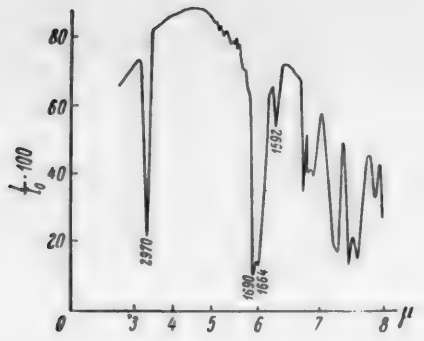


Fig. 1.

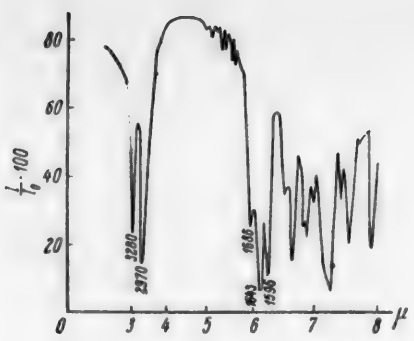


Fig. 2.

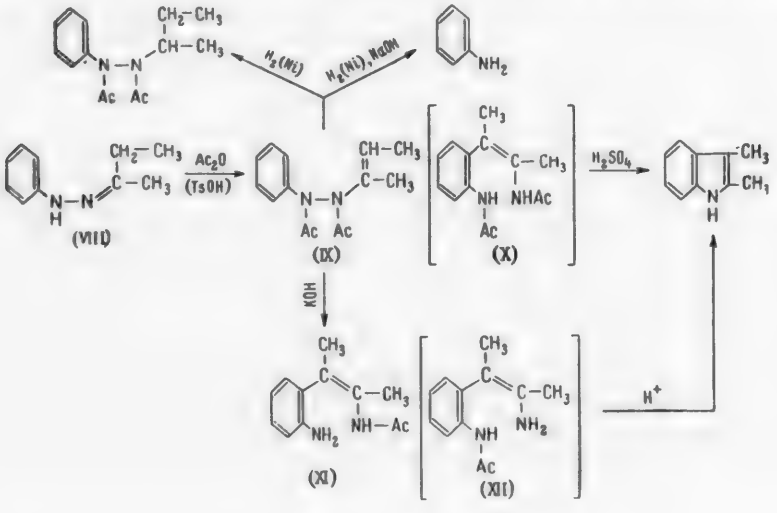
in the reaction product. The position is altered markedly if the hydrogenation is carried out in an alkaline medium. In these circumstances aniline is formed in quantitative yield at 6 atmos and 80°. The formation of the latter provides indisputable evidence that the substance $C_{14}H_{18}O_2N_2$ has structure (IX) being the diacetyl derivative of the unsaturated hydrazo compound – the first stage (II) of the Robinsons' scheme.

Extremely interesting data were obtained from the alkaline saponification of (IX). In this case no 2,3-dimethylindole is formed either by boiling with aqueous alkali or with alcoholic KOH in the cold, but a substance with the composition $C_{12}H_{16}ON_2$ and m. p. 114.5-115° is formed. This substance contains one acetyl group and active hydrogen and gives a positive isonitrile reaction for a primary amino group.

In the infrared spectrum of this compound (Fig. 2) there is an intensive N–H band at 3280 cm^{-1} and in the region characteristic of double bonds there is a system of three intensive bands: of these, the band at 1686 cm^{-1} is a typical amide band, the band at 1643 cm^{-1} can be related to the deformation vibration of NH_2 groups and that at 1596 cm^{-1} to vibration of the aromatic system of double bonds, the considerable increase in intensity in this case results from the presence of additional conjugation (for example, from a C=C bond outside the nucleus).

2,3-Dimethylindole is formed instantaneously by the action of dilute acids on the compound of m. p. 114.5-115° in the cold. This reaction takes place so easily that attempts to diazotize this compound were unsuccessful: closing of the indole ring occurs so rapidly that the diazo compound cannot be formed. 2,3-Dimethylindole is also obtained together with acetamide on heating the above compound to 150°.

All these data indicate conclusively that the substance of m. p. 114.5-115° is 3-acetylamino-2-(o-aminophenyl)-butene-2 (XI). Formula (XII) is excluded by the stability of the substance under conditions of alkaline saponification, and also because cyclization of (XII) would lead to 1-acetyl-2,3-dimethylindole. Compound (XI) is the acetyl derivative of an unsaturated diamine – the second stage (III) of the Robinsons' scheme.



We have thus succeeded in bringing about an ortho-benzidine rearrangement of the unsaturated hydrazocompound (IX) to the diamine (XI) in an alkaline medium. It should be noted that although the benzidine rearrangement takes place, as a rule, in acidic media, other cases have also been recorded in the literature. The case that has been investigated most is that of the rearrangement of 2,2-hydrazonaphthalene. In 1903 Meisenheimer and Witte [15] showed that on heating the latter with alcoholic alkali 2,2-diamino-1,1-dinaphthyl is formed, and this was explained by a benzidine rearrangement under the action of alkali [16]. Later, in papers by L. G. Krolik and V. O. Lukashevick [17] and by Shine [18] it was established that rearrangement in this case takes place without any chemical influence, probably by alcohol taking part as a catalyst. It is very probable that in our case also the alkali functions only to saponify one of the acetyl groups in (IX), as a result of which the stability of the molecule is broken down (see experiments on the hydrogenation of (IX) in neutral and alkaline media).

This loss of the stabilization imparted by the formation of the diacetyl derivative of the unsaturated hydrazocompound suggests a somewhat different line of investigation of the reaction in the case of asymmetric alkylphenylhydrazone. Thus, for example, the asymmetric methylethyl ketone methylphenylhydrazone on heating with acetic anhydride under the conditions described for the preparation of (IX) gives a mixture of at least two substances of which one $C_{13}H_{15}ON$ with m. p. 126.5-127.5° gives a picrate (m. p. 120.5-121.5°) and a 2,4-dinitrophenylhydrazone (m. p. 277-278°).

The formation of a 2,4-dinitrophenylhydrazone indicates the presence of a keto group in the molecule; at the same time the position of the C=O band in the infrared spectrum of this substance at 1660 cm^{-1} shows that this group occurs on the aromatic nucleus in the para position relative to the point of attachment of the nitrogen atom (cf. the spectra of the o-, m- and p-aminoacetophenones [19]).

In the infrared spectrum there is also a strong band at 1560 cm^{-1} which is normally found in N-heterocyclic compounds with bonds of an "aromatic" nature. All this enables the assumption to be made that this substance is a ketone of the indole series, possibly 5-acetyl-1,2,3-trimethylindole. Work on the study of the behavior of asymmetric methylethyl ketone alkylphenylhydrazones is continuing.

Thus by carrying out the Fischer reaction in acetic anhydride and saponifying the acetyl derivative of the unsaturated hydrazocompound we have succeeded in obtaining, in the acetylated form, both of the intermediate products of this reaction – the unsaturated hydrazine (II) and the unsaturated diamine (III) and the fact that these intermediate products cannot be isolated under the Fischer reaction conditions is explained by the extreme rapidity with which the indole ring forms from the unsaturated diamine (III) in an acidic medium. The case reported by Plieninger [13, 14] is probably explained by the fact that here the unsaturated diamine was precipitated in the form of a difficultly soluble hydrochloride. Our artificial method allowed the Fischer reaction to be "dissected" into three completely separate stages in agreement with the Robinsons' mechanism.

The necessity for a catalyst in the first stage of the Fischer reaction can evidently be considered to have been established since on heating methylethyl ketone phenylhydrazone without toluenesulfonic acid the reaction follows another course with the formation of the acetyl derivative of phenylhydrazine (cf. [20]). As regards the o-benzidine rearrangement the presence of an "acid catalyst" is not necessary in this case. The indole ring-closure reaction is very markedly accelerated in the presence of hydrogen ions but it can be accomplished also by heating sufficiently strongly in a neutral medium.

These considerations provide a good explanation of the catalytic conversion of arylhydrazones to indole derivatives by A. E. Arbuzov [3], and the adducts of hydrazo compounds with acetylenedicarboxylic esters of Diels [21]. It should be mentioned that there are in the literature two cases of the formation of indole derivatives from phenylhydrazones in alkaline media – 2-phenylindole from acetophenone phenylhydrazone on refluxing with a solution of sodium ethylate in alcohol [22] and 2-methylindole under the Kishner reaction conditions [23]. It must therefore be recognized that also the formation of the unsaturated hydrazine (II) is evidently not conclusively connected with the presence of an "acid type" catalyst. However, this assumption requires specific experimental verification.

EXPERIMENTAL

2-(N,N'-Diacetyl-β-phenylhydrazino)-butene-2 (IX). 25 g (0.154 mole) methylethyl ketone phenylhydrazone (b. p. 147-147.5° at 15 mm) was refluxed for 1 hr with 159 g (147 ml, 1.54 moles) acetic anhydride and 0.636 g (0.0037 mole, ~ 2.5 mole%) p-toluenesulfonic acid monohydrate. 0.3 g of crystalline sodium acetate

was added to the hot solution, the acetic anhydride distilled off in vacuo, the residue treated with 80 ml water and the product extracted with ether (4 times with 100 ml). After drying over anhydrous sodium sulfate the ether was distilled off and the residue redistilled in vacuo, a fraction being collected at 167-169° at 1.5 mm. The oil obtained (29.62 g) was dissolved in 15 ml absolute ether, 15 ml hexane was added and the product crystallized at −18°. 27 g (86.8%) of a pale pink crystalline material with m. p. 52-56° was obtained. After recrystallization (from n-hexane or absolute ether) a colorless substance was obtained that became pink on standing. M. p. 57-58°. Fairly good solubility in water, good solubility in alcohol, chloroform and benzene; moderately soluble in ether, dissolves with difficulty in cold n-hexane. Decolorizes bromine water and dilute potassium permanganate solution; gives a negative reaction with Fehling's solution.

Found %: C 68.11, 68.01; H 7.15, 7.00; N 10.84, 10.85; Ac 34.3. $C_{14}H_{18}O_2N_2$. Calculated %: C 68.29; H 7.31; N 11.38; Ac 34.9. No active H detected (Zerewitinoff method).

Acid hydrolysis of the diacetyl derivative (IX). 1 g of 2-(N,N'-diacetyl-β-phenylhydrazono)-butene-2 was refluxed with 15 ml of an aqueous solution (1 : 1) of sulfuric acid for 30 min. On cooling the precipitated material was extracted with ether. After distilling off the latter 0.5 g (85%) of 2,3-dimethylindole was obtained, m. p. 99-102° (from aqueous alcohol). No depression of the melting point was observed on mixing with an authentic sample.

Catalytic hydrogenation of (IX). a) 8 g 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 was hydrogenated in an autoclave over 8 g Raney nickel (W-4) in 100 ml ethyl alcohol at 42 atmos and 60° for 7 hrs. After working up in the usual way and redistilling in vacuo, 7.8 g of a colorless oil was obtained, b. p. 151-155° (1.5 mm). From the results of elementary analysis it was 2-(N,N'-diacetyl-β-phenylhydrazino)-butane.

Found %: C 67.25, 67.15; H 8.09, 8.19; N 11.06, 11.05. $C_{14}H_{20}O_2N_2$. Calculated %: C 67.74; H 8.06; N 11.29.

b) 2.5 g 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 was hydrogenated in an autoclave over 2.5 g Raney nickel (W-4) in a mixture of 20 ml ethyl alcohol and 95 ml of 5% aqueous sodium hydroxide. Pressure 6 atmos, temperature 80°, hydrogenation time 2 hrs. The catalyst was filtered off and the filtrate steam-distilled. The distillate was saturated with sodium chloride and the product extracted with ether. To the residue after distilling off the ether 2.5 ml acetic anhydride and 20 ml water was added. 1.32 g (96%) of a substance with m. p. 112-114° was obtained that gave no depression of the melting point on mixing with an authentic sample of acetanilide.

3-Acetylamino-(2-o-aminophenyl)-butene-2 (XI). a) 3 g 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2 (IX) was refluxed for 2 hrs with 30 ml of a 5% aqueous sodium hydroxide solution. On cooling the mixture was diluted with 50 ml water and the product extracted with ether. After distilling off the latter 2.3 g (92.5%) of an oil that crystallized rapidly was obtained. M. p. 114.5-115° (from 1 : 1 alcohol−water). The product was practically insoluble in water and dissolved readily in the usual organic solvents.

Found %: C 70.45, 70.15; H 7.77, 7.91; N 13.94, 13.28; Ac 21.3; active H (Zerewitinoff method) 0.31, 0.51. $C_{12}H_{16}ON_2$. Calculated %: C 70.50; H 7.84; N 13.72; Ac 21.18; active H 0.49.

b) 0.5 g of the diacetyl derivative (IX) was dissolved in 5 ml of 5% alcoholic potassium hydroxide and kept at room temperature for 24 hrs. The solution was then poured into water and extracted with ether. 0.4 g (95%) of 3-acetylamino-2-(o-aminophenyl)-butene-2 was obtained. M. p. 114-114.5° (from aqueous alcohol).

Conversion of 3-acetylamino-2-(o-aminophenyl)-butene-2 (XI) to 2,3-dimethylindole. a) To a solution of 0.5 g (XI) in 10 ml ethyl alcohol 1 ml of concentrated hydrochloric acid was added. The characteristic order of 2,3-dimethylindole arose immediately. After 5 min 20 ml water was added and the 2,3-dimethylindole was extracted with ether. Yield 0.32 g (90%). M. p. 104.5-106° (from aqueous alcohol). No depression of the melting point was observed on mixing with an authentic sample.

b) To a hot solution of 2 g of the monoacetyl derivative (XI) in 10 ml alcohol, 1 drop of concentrated hydrochloric acid was added. The odor of 2,3-dimethylindole arose instantly. After refluxing for 1 hr the solution was diluted with 40 ml water and the 2,3-dimethylindole was carefully extracted with ether. The ethereal extract was washed with water which was combined with the main aqueous layer. The water was distilled off in vacuo and the residual oil redistilled. B. p. 218-220°. 0.45 g (78%) of acetamide was obtained. After distilling off the ether 1.28 g (91%) of 2,3-dimethylindole was obtained. M. p. 104-106°.

c) 1.4 g 3-acetylamino-2-(o-aminophenyl)-butene-2 was carefully heated in a Wurtz flask, with a thermometer immersed in the material. At about 150° a vigorous reaction suddenly commenced, the temperature rose spontaneously to 220° and a liquid distilled off that crystallized rapidly. This substance redistilled at 220° and had m. p. 81-82°. No melting point depression was observed with a sample of acetamide. Yield of acetamide 0.25 g (62%). The residue in the distillation flask was dissolved in ether and the product was sublimed in vacuo (1.5 mm). Yield of 2,3-dimethylindole 0.83 g (84%). M. p. 102-104.5°.

SUMMARY

1. By means of an artificial method (carrying out the Fischer reaction in acetic anhydride and saponifying the diacetyl derivative of the unsaturated hydrazine) the Fischer reaction has been successfully "dissected" into three stages, corresponding to the three stages (unsaturated hydrazo compound – unsaturated diamine – indole derivative) of the mechanism proposed by G, and R. Robinson.

2. Taking methylethyl ketone phenylhydrazone as an example both intermediate products have been isolated in the acetylated form, their structures were proved and the conditions for conversion to the indole derivative have been studied. Direct evidence has thus been obtained for the correctness of G. and R. Robinson's scheme.

3. It has been shown that the formation of the unsaturated hydrazine takes place in the presence of a catalyst of an acidic character; the ortho-benzidine rearrangement does not absolutely require the presence of such a catalyst but can take place in an alkaline medium; the formation of the indole ring proceeds very rapidly when catalyzed by hydrogen ions but it can also be accomplished thermally.

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THE SYNTHESIS OF TROPANE-3-α-OL, TROPINE

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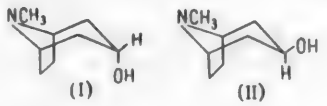
I. K. Sarycheva and N. A. Preobrazhenskii

An important place among the alkaloids is occupied by representives of the tropane group – cocaine, atropine, tropine and also natural and synthetic derivatives. The presence of substituents on the pyrrolidine-piperidine grouping gives a wide possibility of the existence of tropane alkaloids in different stereoisomeric forms. Thus, for cocaine four configurations are known and correspondingly there are four racemic isomers. It has been established that allococaine, allopseudococaine and tropine, synthesized in 1956, are derivatives of tropane-3-α-ol, tropine (I) whereas the basis of natural cocaine and pseudococaine and pseudococaine is the pseudotropine structure (II) [1].



(I) (II)

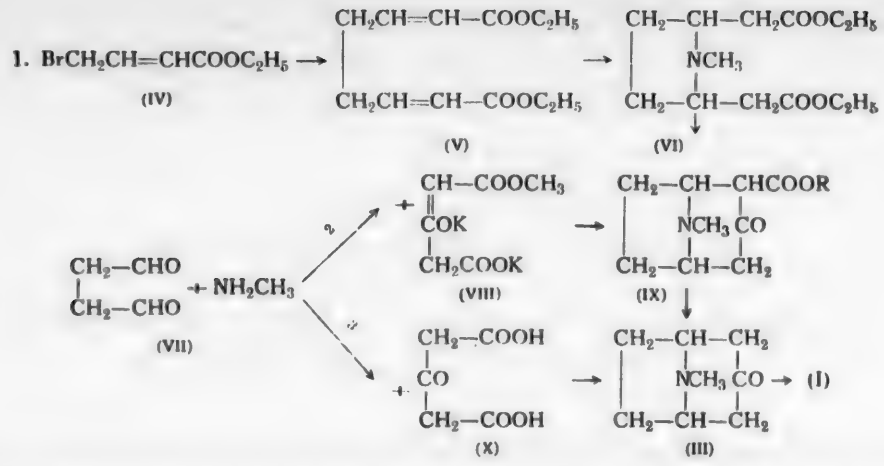
Both forms of tropanol-3 (I and II) have been prepared by a number of authors by reduction of the corresponding ketone, tropanone (III). As the investigations showed, in the formation of one isomer or the other an important role is played not only by the choice of hydrogenating agent but also by the reaction conditions. By the use of sodium amalgam pseudotropine (II) is formed in predominating quantity [2], whereas the use of zinc dust and hydriodic acid leads to a mixture of pseudotropine (II) and tropine (I) [3]. According to the patent literature electrochemical reduction on lead electrodes in an acidic medium gives pseudotropine (II) [4], and under analogous conditions but in an alkaline medium the reaction product is tropine (I) [5].

The present paper describes a stereo-directed reduction of tropanone (III) to tropine (I) accomplished by us. For the preparation of the starting material, previously published methods [6] were used, with the introduction of a number of modifications. We carried out the synthesis of tropanone (III) in accordance with three schemes.

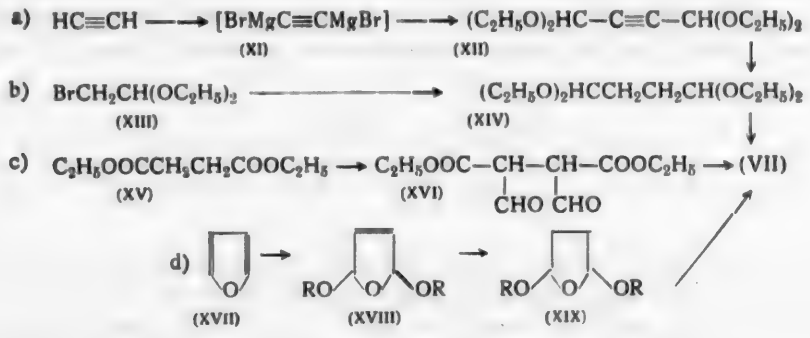
1. In contrast to P. Karrer and G. Alagil [6], who suggested this scheme, ethyl γ-bromocrotoniate (IV) was condensed to ethyl octadiene-2,6-dioate-1,8 (V) with a zinc-copper couple [7] and not with silver. Furthermore the ester of N-methylpyrrolidine-α,α'-diacetic acid (VI) was prepared directly from the ester (V) by the action of methylamine, eliminating the hydrogen bromide addition stage.

2. The method described in the literature for the preparation of the tropinonecarboxylic ester (IX), starting from succindialdehyde (VII), methylamine hydrochloride and the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII) [8], was improved by us in that we found a method of determining the end of the reaction by the formation of the reineckate. The conversion of the tropinonedicarboxylic acid ester was carried out by the usual method [9].

3. The method of G. Gal, I. Simoniy and D. Tokar [10] was used to prepare tropinone (III) in one stage (see scheme on top of following page).



The succindialdehyde (VII) necessary for the synthesis of tropinone (III) we again prepared by a number of methods:



a) From Iotsich's complex (XI) by a method developed by one of us [11] into which improvements were introduced enabling the yield of succindialdehyde ethyl diacetal (XIV) to be increased.

b) For reacting bromoacetaldehyde ethyl acetal (XIII) with sodium, diethyl ether containing peroxidic compounds was used as solvent in accordance with published directions [12]. According to our observation, in spite of the reference quoted, keeping the reaction mass for more than 30 hrs leads to a lowering of the yield of succindialdehyde ethyl diacetal (XIV).

c) This method of synthesizing succindialdehyde was worked out by us for the first time. There is in the literature only an indication of an analogous scheme of synthesis [13].

d) It was found in the present work that in the preparation of dimethoxydihydrofuran (XVIII) the alkoxylation reaction [14] can be carried out in the absence of a solvent.

With the object of finding conditions for the stereo-directed reduction of tropinone (III) to tropine (I) we examined a number of methods – reduction with sodium amalgam, electrolytic and catalytic reduction under various conditions. Only by reduction with Raney nickel catalyst at 60 atmos and 20° did we succeed in preparing tropine (I) free from pseudotropine (II). This synthetic tropine was shown to be identical with tropine isolated from the natural alkaloid atropine.

EXPERIMENTAL

Ethyl octadiene-2,6-dioate-1,8 (V). To a suspension of 17.2 g of freshly prepared zinc-copper couple [7] in 28 ml anhydrous dioxan, heated to 80°, 2 ml of a solution of 40 g ethyl γ-bromocrotonate (IV) in 56 ml dioxan was added, together with a small crystal of iodine. After the appearance of a definite turbidity in the liquid (about 50 min) the remainder of the solution was added dropwise at 80-85°. The reaction mixture was then refluxed for

1.5 hr and treated with 100 ml sulfuric acid (d^{20}_4 1.032), after cooling to 0°. The precipitate was filtered off and washed with 100 ml water. The combined filtrates were extracted with 250 ml ether. The resulting extract was washed with 10% sodium thiosulfate solution, neutralized with a suspension of sodium bicarbonate in water and dried over sodium sulfate. The residue after the removal of ether was redistilled. Yield 4.92 g (20.9%).

B. p. 97-99° (0.3 mm), d^{20}_4 1.042, $n^{20}D$ 1.4604, MR_D 59.55. $C_{12}H_{18}O_4$ F 2. Calculated 59.99. Found %: C 63.92; H 8.23. $C_{12}H_{18}O_4$. Calculated %: C 63.69; H 8.02.

Diethyl N-methylpyrrolidine-α,α'-diacetate (VI). Methylamine, dried over potassium hydroxide, was passed into 7 ml absolute ethyl alcohol to a weight increase of 0.30 g. 4.0 g diethyl octadiene-2,6-dioate-1,8 (V) dissolved in 5 ml ethyl alcohol was added to the solution obtained. The reaction mixture was kept at room temperature for 144 hrs. The solvent was then distilled off and the residue redistilled. Yield 2.9 g (63.7%).

B. p. 110-112° (0.33 mm), d^{20}_4 1.0740, $n^{20}D$ 1.4610, MR_D 65.70. $C_{13}H_{21}O_4N$. Calculated 65.28.

Ethyl tropinonecarboxylate (IX, R = C_2H_5). 2.0 g diethyl N-methylpyrrolidine-α,α'-diacetate (VI) was added dropwise over a period of 10 min to sodium ethylate prepared from 0.22 g sodium and 20 ml ethyl alcohol. The reaction mixture was refluxed for 2 hrs and then after cooling to 0° 20 ml of ice-water was added and the mixture was extracted with 150 ml ether. The aqueous layer was acidified with hydrochloric acid (d^{20}_4 1.047) and after extraction with 150 ml ether it was neutralized with sodium bicarbonate and extracted with 100 ml ether and 100 ml benzene. The combined extracts were dried over sodium sulfate. The solvent was distilled off. 0.9 g of the ethyl tropinonecarboxylate obtained was converted to the picrate. M. p. 133-135.5°.

Found %: N 12.85, 12.88. $C_{17}H_{20}O_{10}N_4$. Calculated %: N 12.75.

Acetylenedialdehyde ethyl diacetal (XII). Purified acetylene was passed for a period of 12 hrs through a solution of ethylmagnesium bromide prepared from 24.3 g magnesium and 76.2 ml ethyl bromide in 200 ml absolute ether. To the resulting grey mass 176 ml ethyl orthoformate was added over a period of 1 hr with vigorous stirring. A precipitate was formed to which 300 ml dry benzene was added. The ether was then distilled from the mixture obtained and the commencement of the reaction, which is accompanied by frothing, was awaited, whereupon the warming was discontinued. After 30 min the reaction mixture was cooled to 0°, treated with a saturated solution of ammonium chloride to pH 6 and extracted with 450 ml ether. The combined extracts were dried over potassium carbonate and redistilled after removal of the solvent. Yield 102 g (75.4% calculated on the magnesium).

B. p. 117-118° (7 mm), m. p. 21-22°, d^{20}_4 0.9586, $n^{20}D$ 1.4309, MR_D 62.10. $C_{12}H_{22}O_4$ F. Calculated 62.18. Found %: C 62.48, 62.67; H 9.71, 9.71. $C_{12}H_{22}O_4$. Calculated %: C 62.57; H 9.71.

Succindialdehyde ethyl diacetal (XIV). 50.3 g acetylenedialdehyde ethyl diacetal (XII) was hydrogenated in 30 ml ethyl alcohol in the presence of 10 g Raney nickel catalyst at an initial pressure of 70 atmos and 24°. By the end of the reaction the pressure had fallen to 58 atmos. The catalyst was filtered off. The residue after the ether was distilled off, was redistilled. Yield 48.9 g (93.2%). B. p. 120-122° (20 mm).

Found %: C 61.24, 61.35; H 10.98, 11.30. $C_{12}H_{26}O_4$. Calculated %: C 61.48; H 11.19.

Succindialdehyde (VII) from succindialdehyde ethyl diacetal (XIV). 10 g succindialdehyde ethyl diacetal was stirred for 1 hr with 95 ml 0.1 N sulfuric acid. The solution was then neutralized with sodium bicarbonate, salted out with calcium chloride and extracted with 300 ml ether. The ethereal extract was dried over sodium sulfate. After removal of the solvent the residue was redistilled. Yield 1.3 g (34.8%).

B. p. 62-63° (12 mm), d^{20}_4 1.0624, $n^{20}D$ 1.4265, MR_D 20.80. $C_4H_6O_2$. Calculated 20.69.

Succindialdehyde ethyl diacetal (XIV) from bromoacetaldehyde ethyl acetal (XIII). To 10.6 g sodium wire, submerged in 200 ml absolute ether containing peroxidic compounds, 87 g bromoacetaldehyde ethyl acetal (XIII) [b. p. 58-60° (12 mm), d^{20}_4 1.3452, $n^{20}D$ 1.4592, MR_D 40.07] was added over a period of 2 hrs. The formation of a yellowish-brown precipitate, accompanied by the evolution of heat, was observed. After stirring for 48 hrs 100 ml ice-water was added to the reaction mixture to dissolve the precipitate. The upper layer was removed and the lower extracted with 100 ml ether. The combined extracts were treated with 50 ml of a 20% aqueous solution of ferrous sulfate, washed with 45 ml water and dried over calcium chloride. After distilling off the solvent the residue was redistilled. Yield 5.27 g (10.2%).

B. p. 116-117° (20 mm), d^{20}_4 0.9168, $n^{20}D$ 1.4151, MR_D 64.01; calculated 64.19. Found %: C 61.03, 61.26; H 11.32, 11.37. $C_{12}H_{26}O_4$. Calculated %: C 61.51; H 11.19.

Succindialdehyde (VII) from ethyl diformylsuccinate (XVI). To 36.7 g sodium wire under 150 ml dry toluene 140 g diethyl succinate (XV) (b. p. 114.5-118° for 25 mm) and 144 g ethyl formate were added over a period of 30 min. The mixture was allowed to stand at room temperature for 50 hrs, by which time the sodium had completely reacted with the compounds stated. 150 g crushed ice was then added to the reaction mixture over a period of 15 min causing the formation of two layers. The lower layer was separated and extracted with 300 ml toluene. The combined toluene extracts were washed with 150 ml ice-water and discarded. The aqueous part of the reaction mixture was neutralized with dilute (d^{20}_4 1.066) sulfuric acid. The precipitate was filtered off and extracted with 300 ml toluene. The toluene was distilled off from the extracts obtained. The residue (150 g) which was a heavy, light brown liquid was heated to boiling with a 20% aqueous oxalic acid solution in a current of nitrogen, omitting the purification stage. Evolution of carbon dioxide was observed. Heating was continued until the oily layer disappeared (4 hrs). The cooled reaction mixture was neutralized with a saturated aqueous sodium bicarbonate solution. The precipitate was filtered off, the filtrate saturated with calcium chloride, extracted with 400 ml ether and the combined extracts dried over sodium sulfate. The residue was redistilled after the solvent had been distilled off. Yield 8.9 g (13.1% calculated on the diethyl succinate).

B. p. 69.5-71° (25 mm), d^{20}_4 1.0659, $n^{20}D$ 1.4260, MR_D 20.65; calculated 20.69. Found %: C 55.63; H 7.04. $C_4H_6O_2$. Calculated %: C 55.80; H 7.02.

2,5-Dimethoxydihydrofuran (XVIII, R = CH_3). To a solution of 28.3 g furan (b. p. 31.5-32° at 756 mm) in 210 ml anhydrous methyl alcohol cooled to −40°, 73.5 g bromine dissolved in 300 ml methyl alcohol cooled to −40° was added dropwise with stirring. The addition was carried out at a rate such that the temperature of the reaction mixture did not exceed −25° (about 1 hr). After maintaining these conditions for 30 min a current of dry ammonia was passed into the reaction mixture to a pH of 6 and stirring was continued at −5° until the color disappeared (about 1 hr) after which ammonia was again passed in to pH 8. The methyl alcohol was distilled off in vacuo (20-30 mm). The precipitate that separated was filtered off and washed with 90 ml methylene dichloride. The residue was redistilled after removal of the solvent. Yield 39 g (72.1%).

B. p. 34-36° (3 mm), d^{20}_4 1.0730, $n^{20}D$ 1.4350, MR_D 31.65. $C_6H_{10}O_3$ F. Calculated 32.17. Found %: C 55.46, 55.14; H 7.48, 7.51. $C_6H_{10}O_3$. Calculated %: C 55.37; H 7.74.

2,5-Diethoxydihydrofuran (XVIII, R = C_2H_5). To a mixture of 34 g furan, 100 ml absolute ether and 150 ml absolute ethyl alcohol cooled to −35°, a solution of 28 ml bromine in 350 ml ethyl alcohol cooled to −40°, was added dropwise with stirring over a period of 1 hr, taking care that the temperature did not exceed −25°. After maintaining this temperature for 30 min dry ammonia was passed in to pH 6, stirring was continued at −5° until the color disappeared and ammonia was again passed in to pH 8. The precipitate was filtered off and washed with 75 ml absolute ether. The residue was redistilled after removal of the solvent. Yield 54.9 g (69.5%).

B. p. 46-48° (5 mm), d^{25}_4 1.0017, $n^{25}D$ 1.4310, MR_D 40.86. $C_8H_{14}O_3$ F. Calculated 41.41. Found %: C 60.68, 61.05; H 8.56, 8.80. $C_8H_{14}O_3$. Calculated %: C 60.80; H 8.86.

2,5-Dimethoxytetrahydrofuran (XIX, R = CH_3). 126 g 2,5-dimethoxydihydrofuran (XVIII, R = CH_3) was hydrogenated in the presence of 13 g Raney nickel catalyst at room temperature and atmospheric pressure, with mechanical stirring. After 22 liters of hydrogen had been absorbed in 6-8 hrs the catalyst was filtered off and washed with 50 ml anhydrous methyl alcohol. The residue after the solvent was distilled off, containing 4-6% dimethoxytetrahydrofuran was combined with the main bulk and redistilled. Yield 109.4 g (85.5%).

B. p. 53-54° (22 mm), d^{25}_4 1.022, $n^{25}D$ 1.4158, MR_D 32.45; calculated 32.63. Found %: C 54.50, 54.49; H 9.11, 9.33. $C_6H_{12}O_3$. Calculated %: C 54.53; H 9.15.

2,5-Diethoxytetrahydrofuran (XIX, R = C_2H_5). Hydrogenation of 2,5-diethoxydihydrofuran (XVIII, R = C_2H_5) was carried out under the conditions used for the preparation of 2,5-dimethoxytetrahydrofuran. 44.2 g 2,5-diethoxydihydrofuran and 5 g Raney nickel catalyst were used. Yield 36.4 g (81.3%).

B. p. 67-69° (15 mm), d^{25}_4 0.9670, $n^{25}D$ 1.4173, MR_D 41.69; calculated 41.87. Found %: C 59.83, 58.73; H 10.05, 10.11. $C_8H_{16}O_3$. Calculated %: C 59.97; H 10.06.

Dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII). 46.8 g of the dimethyl ester of acetonedicarboxylic acid was added, with vigorous mechanical stirring, to a mixture of 240 g of 50% aqueous potassium hydroxide and 138 ml methanol cooled to −5°, whereupon the temperature of the reaction mixture rose spontaneously to 15°. Cooling was then discontinued and the temperature was brought to 25° in 20-30 min. After maintaining these conditions for 10 min the mixture obtained was again cooled to 0° and 45 ml ether was added. The precipitate that formed was filtered off, washed with 45 ml methanol and 100 ml ether cooled to 0° and dried in a vacuum desiccator. Yield 57.2 g (90.1%).

5.3 ml 0.1 N hydrochloric acid was required for the titration of 0.1 g of the substance obtained. After boiling the sample taken for neutralization for 30 min a further 2.9 ml was required (total 8.2 ml).

Calculated on the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid. ($C_6H_6O_5K_2$) requires 8.47 ml 0.1 N hydrochloric acid.

Methyl tropinonecarboxylate (IX, R = CH_3). Experiment 1. For the synthesis of the base and the hydrochloride 13.7 g dimethoxytetrahydrofuran (XIX, R = CH_3) was added (in one lot) to 116 ml 1 N hydrochloric acid, heated to 80° and the mixture was stirred at this temperature for 20 min. The reaction mixture was cooled rapidly to 0°, after which were added successively 88 ml 1 N hydrochloric acid, 38 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII), 106 ml of a 12% aqueous solution of sodium citrate and 10.9 g methylamine hydrochloride. The resulting mixture was stirred at 30° for 4 hrs.

The course of formation of the methyl tropinonecarboxylate (IX, R = CH_3) was followed by a gravimetric method, by determining it as the reineckate. For this purpose a 2 ml test portion of the reaction mixture was mixed with 25 ml of a 1% aqueous solution of Reinecke salt, acidified with hydrochloric acid (d^{20}_4 1.19) and brought to a volume of 50 ml with distilled water. The precipitate formed after 60 min was filtered off and dried in a vacuum desiccator. M. p. 156-158° (decomp.).

Found %: N 18.93, 18.80. $C_{14}H_{22}O_3N_7S_4Cr$. Calculated %: N 18.99.

The reaction mixture was cooled to 0°, saturated with 180 g potassium carbonate and extracted with benzene (4 times with 150 ml) by stirring for 10-15 min. The residue, after removal of the solvent, was redistilled. Yield 11.5 g (56.2% calculated on the dimethoxytetrahydrofuran, XIX, R = CH_3). B. p. 85-88° (0.2 mm).

Found %: N 7.10, 6.95. $C_{10}H_{15}O_3N$. Calculated %: N 7.09.

Hydrochloride of methyl tropinonecarboxylate, m. p. 172-173°.

Found %: C 51.58, 51.39; H 7.06, 6.70; N 6.17, 6.13. $C_{10}H_{16}O_3NCl$. Calculated %: C 51.39; H 6.9; N 5.99.

Experiment 2. For the preparation of the hydrate of the base, 66 g dimethoxytetrahydrofuran (XIX, R = = CH_3) was added to 500 ml hydrochloric acid heated to 80° and stirred at that temperature for 20 min, after which the mixture was cooled rapidly to 10°. To the solution of succindialdehyde (VII) formed was added consecutively 484 ml 1 N hydrochloric acid, 165 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII), 49.5 g sodium acetate and 48.4 g methylamine hydrochloride, and the reaction mixture was stirred for 4 hrs at 29-31°. Then after cooling to 10° it was acidified to pH 4 with hydrochloric acid (d^{20}_4 1.19), extracted with 200 ml ether, saturated with 500 g potassium carbonate and finally extracted with 1000 ml benzene. After removal of the solvent in vacuo 79.2 g of a brown, oily residue was obtained, from which the methyl tropinonecarboxylate base (IX, R = CH_3) was isolated in the form of the hydrate . For this purpose 19.5 ml distilled water was added to the crude methyl tropinonecarboxylate (IX, R = CH_3). The mass rapidly solidified on trituration. The crystals formed were filtered off, washed with 75 ml absolute ether and recrystallized from methanol. Yield 68.4 g (56.1% calculated on the dimethoxytetrahydrofuran, XIX, R = CH_3). M. p. 94-96°.

Found %: N 5.91, 5.82. $C_{10}H_{15}O_3N \cdot 2.5H_2O$. Calculated %: N 5.78.

Experiment 3. For preparing the base 15 g succindialdehyde ethyl diacetal (XIV) was stirred for 1 hr with 140 ml sulfuric acid (d^{20}_4 1.030) at room temperature. Then to the reaction mixture, cooled to −5°, was added consecutively a solution of 20 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylate, previously neutralized at 0°, 7.4 ml hydrochloric acid (d^{20}_4 1.19), 7.9 g sodium citrate and 6 g methylamine hydrochloride. The resulting mixture was stirred at 30° for 4 hrs, saturated at 0-5° with 150 g potassium carbonate and

extracted with 600 ml benzene. The residue, weighing 10.1 g, crystallized out after the solvent had been distilled off in vacuo (20 mm). For purification it was recrystallized from methyl alcohol. Yield 7.45 g (59% calculated on the succindialdehyde ethyl diacetal (XIV)). M. p. 106-107°.

Found %: C 61.15, 61.10; H 7.44, 7.65. $C_{10}H_{15}O_3N$. Calculated %: C 60.89; H 7.66.

Experiment 4. For the synthesis of the hydrate and the free base, to a solution of 4.3 g succindialdehyde (VII) in 100 ml 1 N hydrochloric acid was added 18.9 g of the dipotassium salt of the monomethyl ester of acetonedicarboxylic acid (VIII) and 4 g sodium acetate or 50 ml of a 12% aqueous solution of sodium citrate (pH 4.5-5), after which 5.35 g methylamine hydrochloride was added. The solution obtained was stirred for 4 hrs at 30-31°. The reaction mixture was then cooled to 10°, saturated with potassium carbonate and extracted with 150 ml benzene. The solvent was distilled from the extract after drying over sodium sulfate and the methyl tropinonecarboxylate base (IX, R = CH_3) was isolated in the form of the hydrate. Yield 8.63 g (61.3%). M. p. 94-96°.

On drying in a vacuum desiccator over phosphorus pentoxide the hydrate lost water and was converted to the base (IX, R = CH_3). M. p. 106.4-107.6°.

Found %: C 60.78, 61.12; H 7.91, 7.65; N 7.14, 7.04. $C_{10}H_{15}O_3N$. Calculated %: C 60.89; H 7.66; N 7.09.

Tropinone (III). 114 g dimethoxytetrahydrofuran (XIX, R = CH_3) was added to 862 ml 1 N hydrochloric acid, heated to 80°, and stirred at this temperature for 20 min. 176 g acetonedicarboxylic acid (X) was then dissolved gradually in the reaction mixture after cooling the latter to 10°, after this the pH was brought to 5, at 5-10°, by means of potassium carbonate (about 195 g), and 900 ml of a 12% aqueous solution of sodium citrate and 81 g methylamine hydrochloride was added. The resulting mixture was stirred at 30°. The course of formation of tropinone (III) was followed by a gravimetric method by determining it as the reineckate [10] (see experiment 1). M. p. 180-182 (decomp.).

After 4 hrs the content of tropinone in the solution analyzed was 75% of theory, calculated on the dimethoxytetrahydrofuran (XIX, R = CH_3). The reaction mixture was then cooled to 0°, saturated with 750 g potassium carbonate and extracted with benzene (4 times with 900 ml). The residue after removal of the solvent was redistilled. Yield 67.9 g (56.56% calculated on the dimethoxytetrahydrofuran, XIX, R = CH_3). B. p. 69-71° (4 mm), m. p. 41-42°.

Found %: C 69.05, 68.91; H 9.30, 9.18; N 9.82, 9.90. $C_8H_{13}ON$. Calculated %: C 69.03; H 9.41; N 10.06.

Tropine (I). Experiment 1. 29.7 g tropinone (III) was dissolved in 150 ml anhydrous methyl alcohol and hydrogenated in the presence of 4.5 g Raney nickel catalyst at room temperature and 60 atmos for a period of 4 hrs. The catalyst was filtered off and washed with 30 ml anhydrous methanol. The residue after removal of the solvent was redistilled. Yield 24.35 g (80.67%). B. p. 102-104° (7 mm).

Found %: C 68.13, 68.22; H 10.43, 10.58; N 10.10, 10.12. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.71; N 9.91.

Experiment 2. 20 g tropinone (III) was hydrogenated under the conditions of experiment 1. The residue after removal of methyl alcohol was dried by adding dry benzene and subsequent vacuum distillation (15-30 mm). The tropine obtained, weighing 19.2 g, was recrystallized from ether. Yield 16.4 g (80.84%). M. p. 61-62°.

Found %: C 67.89, 67.99; H 11.07, 10.92; N 9.66, 9.72. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.71; N 9.91.

A mixture of the synthetic tropine (m. p. 61-62°) with tropine (m. p. 59-61°) isolated from the natural alkaloid atropine gave no depression of the melting point.

SUMMARY

1. The spatially directed catalytic hydrogenation of tropinone to tropine has been achieved.

2. It has been established that depending on the reducing agent (reduction by sodium amalgam, electrolytically or by hydrogenation in the presence of Raney nickel catalyst, or platinum or palladium oxide) and on the reaction conditions the tropane-3-ols are obtained with varying relative contents of steric isomers.

3. Methods of preparing esters of tropinecarboxylic acid have been studied.

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REACTIONS OF MAGNESYLAMINES

V. THE MECHANISM OF THE REACTION OF ARYL AMIDATION OF AROMATIC ALDEHYDES BY N,N-BIS-(MAGNESIUM HALIDE)-ARYL AMINES

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To explain the mechanism of the reaction of aryl amidation of aromatic aldehydes by N,N-bis-(magnesium halide)-aryl amines it was first necessary to study the ratio of magnesylamines to aldehydes, since this question has not been considered in the literature. The first experiments were carried out with monomagnesylamines. They showed that phenylbromomagnesylamine (I) reacts energetically with benzaldehyde, but after decomposition of the reaction mass there was separation again into aniline and benzaldehyde, and only small amounts of benzanilide were formed. We could assign to the magnesium organic complex (II) formed by the reaction of (I) with benzaldehyde the structure of a bromomagnesium alcoholate of a hydroxyamine.

$$\underset{\text{(I)}}{C_6H_5NHMgBr} + C_6H_5CHO \rightarrow \underset{\text{(II)}}{C_6H_5CH(OMgBr)NHC_6H_5}$$

The halogenomagnesium alcoholate nature of this complex well explains the hydrolysis to form aniline and benzaldehyde and also its inability to react with ethyl benzoate (experiment 2a). Along with these experiments it was shown that monomagnesylamines in general, and also the magnesium organic complex (II) (experiment 2b), cannot catalyze the reaction of aryl amidation of aldehydes.

The small amount of benzanilide which we did succeed in obtaining in the previous experiment evidently came from the presence of dimagnesylamine in the reagent. The latter can be formed along with (I) in the reaction between aniline and ethylmagnesiumbromide.

The assumption that monomagnesylamine cannot catalyze the reaction of aryl amidation of aldehydes also was confirmed experimentally in the reaction with N-ethylaniline. Ethylaniline gives with ethylmagnesiumbromide only monomagnesium derivatives which in the experiment with benzaldehyde give no N-ethylanilide of benzoic acid.

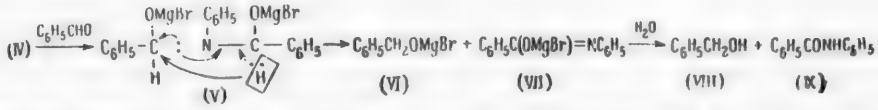
Further studies were carried out toward explaining the role of dimagnesylamines in the aryl amidation of aldehydes. Thus, when equivalent amounts of N,N,-bis-(bromomagnesium)-aniline (III) react with benzaldehyde, the yield of benzanilide rises to 3%. The reaction occurs by the following scheme:

$$\underset{\text{(III)}}{C_6H_5N(MgBr)_2} + C_6H_5CHO \rightarrow \underset{\text{(IV)}}{C_6H_5CH(OMgBr)N(MgBr)C_6H_5}$$

The magnesium organic complex (IV) thus formed has both a halogenomagnesium alcoholate and a halogenomagnesylamine character. On hydrolysis it splits into aniline and benzaldehyde. As a halogenomagnesylamine derivative it reacts with ethyl benzoate.

We note that when we turn from the experiment with monomagnesylamine to the experiment with dimagnesylamine, the yield of benzanilide rises from 1 to 3%, that is, 3 times. This is direct evidence that aryl amidation of the aldehyde goes only through the dimagnesylamine.

Earlier [1] it was shown that the most successful aryl amidation occurs when 1 mole of dimagnesylamine reacts with 2 moles of benzaldehyde. Due to its halogenomagnesylamine character, complex (IV) can react with a new molecule of aldehyde* to form the halgoenomagnesium alcoholate of a dihydroxyamine (V), in which also an oxidation-reduction reaction occurs.



The thus formed halogenomagnesium alcoholate of benzyl alcohol (VI) and the magnesium halide derivative of the lactim form of benzaldehyde (VII) are further decomposed into the alcohol (VIII) and benzanilide (IX).

In our work [1] the aryl amidation of aldehydes with N,N-bis-(halogenomagnesium)-arylamines was assigned to the type of oxidation-reduction reactions although only aryl amides were isolated from the final reaction product. In the present work in special experiments we have isolated and identified a second end product of the reaction, benzyl alcohol (experiment 6). Thus, our assumption as to the oxidation-reduction nature of this reaction has been confirmed experimentally. Just as in the case of the Cannizzaro reaction [2] we can probably admit that in complex (V) splitting of the bond occurs homolytically. Hence, in an oxidative-reductive transformation of complex (V), the boiling point and chemical nature of the solvent in which the reaction is carried out should have great influence.

EXPERIMENTAL

1. Reaction of phenylbromomagnesylamine (I) with benzaldehyde in the ratio 1 : 1. To 0.05 g-mole of ethylmagnesium bromide obtained in the usual way from 5.45 g ethyl bromide and 1.2 g magnesium in 30 ml of ether was added with good cooling and stirring a solution of 4.66 g (0.05 g-mole) of aniline in 15 ml of ether. To the resulting (I) was added a solution of 5.3 g (0.05 g-mole) of benzaldehyde in 20 ml of ether. Energetic boiling occurred. The contents of the flask were heated for 2 hrs on the water bath and the magnesium organic complex (II) was decomposed with dilute hydrochloric acid. The ether layer was separated and the ether and also the unreacted benzaldehyde were distilled off with steam. In the distillation flask there remained 0.1 g of benzanilide (1% calculated on the aniline taken in the reaction). Needles from toluene, m. p. 163° [3]. Aniline was isolated in the usual way from the aqueous acid layer.

2. Reaction of the magnesium organic complex (II) with ethyl benzoate and benzaldehyde. a) The magnesium organic complex (II) obtained by the method of the previous experiment was treated with 3.75 g (0.025 g-mole) of ethyl benzoate in 15 ml of ether (boiling of the ether did not occur). The reaction mass was heated 2 hrs on the water bath, decomposed with dilute hydrochloric acid, and treated further as in experiment 1. Yield of benzanilide 0.1 g (1%).

b) The reaction between (II) and benzaldehyde in equimolar quantities was carried out in exactly the same way. The ether did not boil when the benzaldehyde was added. After decomposition of the reaction mass we isolated benzaldehyde, aniline, and 1% benzanilide.

3. Reaction of phenylethylbromomagnesylamine with benzaldehyde in the ratio 1 : 1. To 0.05 g-mole of ethyl bromide was added 6.05 g (0.05 g-mole) of N-ethylaniline in 20 ml of ether and the mixture was heated for 30 min on the water bath. Then we added 5.03 g (0.05 g-mole) of benzaldehyde in 20 ml of ether; boiling of the ether occurred. In conclusion the reaction mass was heated 2 hours on the water bath, decomposed by dilute hydrochloric acid, and treated further as in experiment 1. As a result, we isolated benzaldehyde and ethylaniline. Formation of the N-ethylanilide of benzoic acid was not observed.

4. Reaction of N,N-bis-(bromomagnesium)-aniline (III) with benzaldehyde in 1 : 1 ratio. To 0.05 g-mole of N,N-bis-(bromomagnesium)-aniline, obtained by the method of [4], with good cooling and stirring we slowly added a solution of 6.05 g (0.05 g-mole) of benzaldehyde in 20 ml of ether. The contents of the flask were heated 2 hrs on the water bath and the magnesium organic complex (IV) was decomposed with dilute hydrochloric acid and then treated as in experiment 1. We obtained 0.3 g of benzanilide (3%).

* Experiments describing the reaction between dimagnesylamines and aldehydes in the ratio 1 : 2 were published in the previous communication.

5. Course of the reaction between the magnesium organic complex (IV) and ethyl benzoate. The magnesium organic complex (IV) obtained by the method of the previous experiment was treated with a solution of 3.75 g (0.025 g-mole) of ethyl benzoate in 20 ml of ether. Energetic boiling of the ether occurred. In conclusion the reaction mass was heated for 2 hrs on the water bath and then treated as in the previous experiments. Yield 1.2 g (12.2 %) of benzanilide.

6. Isolation and identification of benzyl alcohol (VIII). The experiment was carried out by process B, described in the previous communication. Starting substances: 31.8 g (0.3 g-mole) of benzaldehyde in 60 ml of dry pyridine and 0.15 g-mole of dimagnesylamine, obtained from 32.4 g (0.3 g-mole) of ethyl bromide. 7.2 g (0.3 g-mole) magnesium, and 13.8 g (0.15 g-mole) of aniline. The reaction mass was decomposed with dilute hydrochloric acid and the benzanilide which separated was filtered and washed with ether. Yield 11.3 g (38.3% calculated on the aniline taken for the reaction). The filtrate was extracted three times with ether, the ether extracts were combined and most of the ether was distilled off. For separation of the unreacted benzaldehyde the residue was shaken 4 times with a 40% solution of sodium bisulfite, 10 ml each time. Then the ether layer was shaken with a solution of sodium bicarbonate (to remove the dissolved sulfurous acid) and dried over sodium sulfate. After removal of the solvent, the residue was distilled at atmospheric pressure and the fraction boiling 201-205° was collected. Yield, 7.1 g (21.9% calculated on the benzaldehyde taken for the reaction). Benzyl alcohol was identified by reaction with hydrobromic acid (formation of benzyl bromide) and by reaction with phenyl isocyanate. The phenylurethane melted at 77-78°. The literature records 78° [5]. A mixed melting point with known phenylurethane showed no depression.

SUMMARY

We have assumed and experimentally established the mechanism of the reaction of aryl amidation of aromatic aldehydes by N,N-bis-(halogenomagnesium)-aryl amines.

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THE OCCURRENCE OF EQUILIBRIUM OF THREE LIQUID PHASES IN TERNARY SYSTEMS

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Until recently stable equilibrium of three liquid phases has been found in ternary systems formed by binary systems with stable phase separation. It has also been shown [1] that equilibrium of three liquid phases can occur in ternary systems which contain a binary system with metastable phase separation. In the case studied, the three-phase liquid equilibrium was also metastable and occurred according to the same scheme as the stable phase separation. Stable equilibrium of three liquid phases in a ternary system containing one or several binary systems with metastable phase separation has not been studied. The study of this type of equilibrium and the method of its formation is the purpose of the present work.

EXPERIMENTAL

We selected for the study of this question the ternary system anthranilic acid–water–benzine. The binary system anthranilic acid–benzine was studied in this work to relate it to systems with metastable phase separation. The system water–benzine belongs to systems with stable phase separation and a very high upper critical point [1]. The system water–anthranilic acid has been studied for stratification [2]. The curve for the metastable phase separation of the system has an upper critical point at 78°, corresponding to 38% anthranilic acid. Thus, the chosen ternary system contains two binary systems with metastable phase separation and one with stable separation.

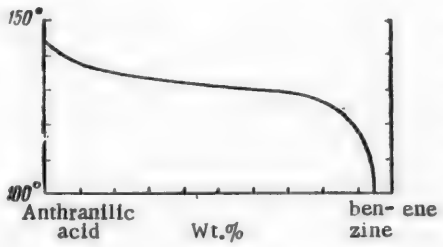

Fig. 1. Equilibrium in the system anthranilic acid–benzine.

TABLE 1

Equilibrium in the System Anthranilic Acid–Benzine

% Anthranilic acid	Temperature of crystallization
5.00	107.0°
20.00	127.0
40.00	130.0
60.00	132.5
80.00	134.5
100.00	145.0

We used the following reagents in the study: C. P. anthranilic acid, m. p. 145°, twice distilled water, and a benzine fraction boiling in the range 90-120°. Equilibrium between two and three liquid phases was studied by the visual-polythermal method of V. F. Alekseev [3] in a sealed glass ampule in an oil thermostat. In the same ampule and thermostat we also studied crystallization in the system anthranilic acid–benzine using an inner heater [4].

The system anthranilic acid–benzine was studied by fusibility (Table 1 and Fig. 1). As Fig. 1 shows, the curve of crystallization of anthranilic acid has a very sloping S-shape and occupies almost all the concentration intervals of the system. Such a form for the crystallization curve should indicate the presence under it of a curve of metastable phase separation. The latter is found at very low temperatures, since experimentally it was not observed with supercooling. Its presence could be shown indirectly, as will be demonstrated below.

The ternary system anthranilic acid–water–benzine was studied by stratification. We studied six polythermal sections through its temperature-concentration prism, going from its anthranilic acid

TABLE 2

Polytherms of the System Anthranilic Acid—Water—Benzine

% Anthranilic acid	Temperature		% Anthranilic acid	Temperature	
	2-phase stratification	3-phase stratification		2-phase stratification	3-phase stratification
Section 1			**Section 2**		
5% benzine, 95% water			20% benzine, 80% water		
49.00	70.0°	—	40.00	—	98.0°
49.50	91.0	—	45.00	—	101.0
50.00	115.0	—	50.00	—	110.0
			55.00	—	116.5
			60.00	—	121.5
			65.00	—	123.5
			70.00	—	121.0
			72.00	—	118.0
			78.00	122.0°	—
			79.00	105.0	—
			79.50	95.0	—
Section 3			**Section 4**		
40% benzine, 60% water			60% benzine, 40% water		
35.00	—	97.0°	35.00	—	95.0°
40.00	—	104.0	40.00	—	106.0
45.00	—	110.0	45.00	—	114.0
50.00	—	116.0	50.00	—	120.0
55.00	—	120.0	55.00	—	123.5
60.00	—	123.0	60.00	—	121.0
65.00	—	124.0	65.00	—	117.0
70.00	—	119.0	70.00	—	112.0
75.00	—	112.0	75.00	—	105.0
80.00	—	105.0	76.00	—	99.0
81.00	—	100.0	84.00	120.0°	—
85.00	119.0°	—	85.00	102.0	—
85.50	108.0	—	85.50	88.0	—
86.00	94.0	—			
Section 5			**Section 6**		
80% benzine, 20% water			98% benzine, 2% water		
35.00	—	100.0°	50.00	93.0°	—
40.00	—	108.0	60.00	109.0	—
45.00	—	115.0	70.00	120.0	—
50.00	—	121.0			
55.00	—	123.5			
60.00	—	115.0			
62.00	—	109.0			
63.00	—	98.0			
80.00	119.0°	—			
82.00	103.0	—			
84.00	90.0	—			

edge to the boundary of the binary system water—benzine (Table 2, Fig. 2). The sections and polytherms were numbered in the order of increasing benzine content in the mixture. In sections 1 and 6 we found equilibrium only between the two liquid phases, in the others, between two and between three liquid phases. As Fig. 2 shows, the polytherm of the two-phase liquid is almost a vertical line. Thus, the reciprocal solubility of the two-liquid phases in the ternary system depends little on temperature. Between these polytherms and the anthranilic acid edge lies a field of unsaturated homogeneous solutions. Between them and the boundary of the system benzine—water lies a field of heterogeneous liquid solutions. The polytherms of the three-phase liquid state are curves with maxima at about the same temperature, 124°. This corresponds to their location on the critical conode of the three-phase liquid equilibrium.

From the experimentally obtained polytherms we constructed the isothermal sections of the prisms of the ternary system anthranilic acid—water—benzine at 100, 110, and 120°. A projection isotherm is shown on the

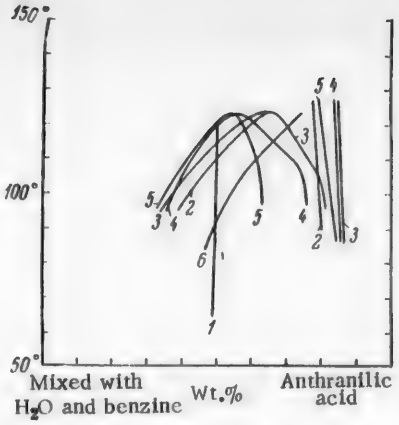

Fig. 2. Polytherms of the ternary system anthranilic acid—water—benzine. Explanation in text.

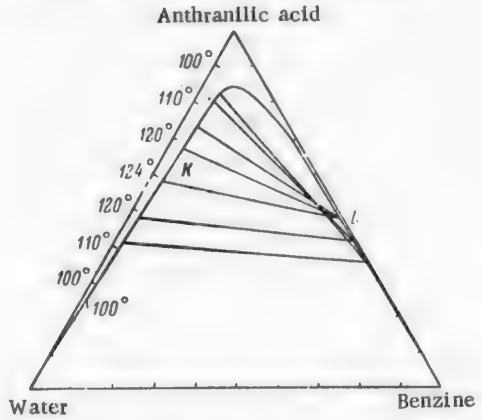

Fig. 3. Isotherms of the ternary system anthranilic acid—water—benzine (KL — critical conode; figures along the sides of the triangle relate to the corresponding conode). Explanation in text.

triangle in Fig. 3, on which is shown the projection of the critical conode KL of the three-phase liquid state. On Fig. 3 the curve of the two-phase liquid state is shown at 100° only; the other two almost agree with it since the liquid phase equilibrium is practically unchanged with temperature. The field of the two-phase liquid state which adjoins the triangle of the three-liquid phases on the side of the binary system anthranilic acid—water is very narrow. Therefore, it was not determined.

In the ternary system anthranilic acid—water—benzine the following processes occur as the temperature is lowered. In the stable state at high temperature, phase separation of the binary system water—benzine is homogenized by anthranilic acid. The content of the latter in the heterogeneous mixture reaches 86%. The system anthranilic acid—water is dominant among the binary systems of the ternary system. At 124° there appears on the binodal curve the critical solution K (composition 67% anthranilic acid, 29.5% water, and 3.5% benzine) and the corresponding solution L (46% anthranilic acid, 1% water, and 53% benzine), and the critical conode KL is formed. When the temperature is lowered the volume of three-phase liquid state develops from the latter. On the isotherm appears the triangular equilibrium of three liquid phases from the side of which to the side of the binary homogeneous system there develops a field of a two-phase liquid equilibrium. In the metastable state at 78° one of the equilibrium fields of two-liquid phases of the ternary system reached the field of binary system anthranilic acid—water. A shift then occurs in the dominant system. The binary system anthranilic acid—benzine becomes dominant. This confirms the idea established earlier that in ternary systems with an equilibrium of three liquid phases the temperature at which the dominating systems change is the critical solution temperature of that binary system which lies between the other two binary systems. As that temperature is lowered further, a third field of a two-phase liquid state of the ternary system reaches the boundary of the binary system anthranilic acid—benzine. In the latter from this moment appears a break in solubility. Because of this the binary system anthranilic acid—benzine must be considered a system with a very low location of upper critical point.

The processes described are analogous to those which occur in the formation of a stable equilibrium of three liquid phases in ternary systems which contain binary systems with stable phase separation. Thus, the polythermal scheme of occurrence and development of stable three phase liquid equilibrium is the same in ternary systems which contain binary systems with stable and metastable phase separation.

SUMMARY

1. We have studied the binary system anthranilic acid—benzine by the fusibility method. We have shown that it belongs to systems with metastable phase separation with a very low position for the upper critical point.

2. We have studied phase separation in the ternary system anthranilic acid—water—benzine. We have found in it a volume of a stable equilibrium of three liquid phases at temperatures below 124° (the critical temperature of the conode). We have found the temperature-concentration boundaries of the area of the three-phase liquid equilibrium and the composition of the corresponding solutions of the critical conode.

3. We have shown that the polythermal scheme of occurrence and development of a stable equilibrium of three liquid phases is the same in ternary systems which contain binary systems with stable and metastable phase separation.

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THE CAUSES OF THE TRANSPOSITION OF METALS IN THE ELECTROMOTIVE FORCE SERIES IN FUSED ELECTROLYTES

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Recently, E. Ia. Gorenbein [1, 2] has considered the question of the causes for the transposition of metals in the electromotive force series. This author has concluded one of his papers as follows. "On the basis of the present knowledge of the structure of liquids, an explanation is given for the causes of transposition of metals in the electromotive force series" [1]. We wish to make some comments on this explanation.

Gorenbein connects many properties of solutions and melts with the formation of "structural groups" which, in his opinion, determine the conductivity and osmotic pressure of solutions, and also assure equilibrium at the metal-solution boundary. As we can conclude from a series of papers by Gorenbein [1-5], these hypothetical "structural groups" are assigned the following properties by him.

1. "Structural groups" have their own intrinsic conductivity, higher than the conductivity of the same ions which do not enter a "structural group."

2. In cryoscopic studies, the "structural groups" behave as separate kinetic particles.

3. Ions in "structural groups" do not have definite potentials.

4. The forces which characterize the formation of "structural groups" are of the same nature as the forces which determine the formation of ionic crystal lattices.

It is a matter of primary interest to determine how far these views of Gorenbein can be considered to be scientifically established and how they relate to the transposition of metals in the electrochemical series.

As is known, the idea of the quasi-crystalline structure of liquids was introduced by Stewart [6, 7] who showed experimentally (roentgenographically) that liquids near the melting point often keep a crystalline structure. Stewart also brought about an understanding of the regularities which he called "cybotactic groups." The quasi-crystalline arrangement of liquids was also experimentally established by Danilov [8], Donat [9], and other authors. At the present time this arrangement of liquids is accepted as being present in areas in which the molecular distributions are similar to but not identical with the crystalline state [10]. Such ideas come chiefly from Frenkel [11] and Danilov [12] who have successfully developed these ideas. The latter especially has shown that quasi-crystalline structures are also found in solutions. At the present time the theory of the quasi-crystalline structure of solutions has been developed by many workers [10, 13-18]. The basic ideas of this theory are the following.

1. In solutions there is a close arrangement and a quasi-crystalline distribution of molecules.

2. In solutions a fluctuation of concentration occurs which differentiates solutions from pure liquids [14].

3. The number of most closely adjacent molecules is determined by a coordination number which is characteristic of the structure of the solution.

4. Reaction between molecules which make up the solution is produced by their general momentum and the distance between them [10].

5. In solution there occur processes of solvation and association which can be considered as intermediate steps in the formation of chemical compounds. Solvation and association either alter the quasi-crystalline structure of the solvent or form a new quasi-crystalline structure with it.

These theoretical ideas are based on experimental data: roentgenographic, optical (light dispersion), thermochemical (calorimetric), and others. It is not hard to see that in the quasi-crystalline theory of solutions there is no place for "structural groups" with properties such as those described by Gorenbein. The structural groups of Gorenbein do not fluctuate and there is no quasi-crystalline formation of a close arrangement for this is not an independent kinetic particle which can change the osmotic pressure. His groups are not associations, for these do not have their own superconductivity. In no case has this been shown. What, then, are the "structural groups" of Gorenbein? We consider what he himself has written. We read the following concerning the intrinsic conductivity of the "structural groups": "We explain the increased corrected molecular conductivity with increased concentration by the rise in the number of structural groups which have their own conductivity. Ions can migrate not only into the structural groups, but also can transfer from one group to another. It seems to us that the conductivity of the structural groups can be compared to the mechanism of conductivity in crystals, with this difference, that in structural groups both cations and anions take part in the transmission of the current" [5].

If the intrinsic conductivity of the "structural groups" is compared to the conductivity of the ions of a crystal, as Gorenbein says, then the statement that the structural groups should be higher than that of the same ions which are not in structural groups contradicts the present theory of the conductivity of the ions of crystals. According to the theory of Frenkel [19], not all the ions share in the conductivity, but only those which under the influence of thermal motion have been torn from their positions, or are so "activated" that they can easily be torn from them. Thus, the greater the defects in the crystal lattice and the more the "free" ions, the higher will be the conductivity. With increase in temperature, there is an increase in the number of "activated" ions and the conductivity rises. As is known, Frenkel has assumed a temperature relation of conductivity for the ions of crystals of

$$\varkappa = A \cdot e^{-\frac{u}{kT}} \qquad (1)$$

Much experimental data on the conductivity of fused salts has shown the correctness of Eq. (1) for them.

Thus we can say that the mechanisms of the conductivity for the ions of crystals and the ions of melts have much in common. If this is so, then it is quite impossible to assert that ions combined in "structural groups" will migrate faster in an electrical field than do "free ions." This clearly contradicts the assumption of Gorenbein of the presence of some sort of structural group which would have a higher conductivity than systems which consist of the same "free" ions.

There is no clarity in the idea of Gorenbein on "structural groups" as independent kinetic particles. On this question Gorenbein writes, "These structural groups in cryoscopic studies behave as separate kinetic particles" [2]. As already mentioned, the existence of these "structural groups" as free kinetic particles does not come from the quasi-crystalline theory of the structure of solutions. In one of his papers, Gorenbein [1] calls his "structural groups" associates. By associates we mean molecular compounds formed from one type of molecules. If "structural groups" are such associates, then why say that he has worked out a new theory of concentrated solutions as if based on the present theory of the liquid state.

Any theory of solutions must establish a theoretical basis for the relation of thermodynamic properties to the concentration of the components. This important element is absent from the discussions of Gorenbein. Following Sakhanov [20, 21] he introduces a correction for the conductivity with viscosity but gives only

$$\varkappa_{\text{corr.}} = \varphi(c), \qquad (2)$$

where $\varkappa_{\text{corr}}$ is the specific conductivity corrected for viscosity. The empirically established form of this function cannot be considered as a new theory of solutions. As was very truly shown by Izmailov [22], such an unconditional correction of conductivity for viscosity cannot be considered proper.

When Gorenbein turns to a consideration of the results of a potentiometric measurement, his "structural groups" acquire new properties. They lose their kinetic mobility and the ions which enter the structural groups and which migrated so strongly in the conductivity measurements, now "do not wish" to exchange with the atoms on the surface of the metal electrode, that is, do not share in transfer of current. Such contradictory properties of the "structural groups" are probably explained by the fact that they exist only as theoretical constructions of Gorenbein. As shown above, ideas of "structural groups" with such properties as Gorenbein ascribes to them are contradictory to the theory of the quasi-crystalline structure of solutions and also to the theory of conductivity of ions of crystals and melts.

In one paper [1] Gorenbein attempts to show that the transposition of metals in the electrochemical series occurs chiefly in solutions with a low dielectric permeability (DP). However, this is not so. It is well known that the electrochemical series is changed in a series of individual salts with common anions and also in solvents with a high DP, for example, in fused salts (NaF, NaCl–KCl–$SrCl_2$, NaBr–KBr, NaI and others) [23]. Gorenbein groundlessly considers aluminum halides as dielectrics which enter the composition of such fused systems, in which their content does not exceed 50 mole%. It is well known that aluminum halides form strong complexes with the halides of other metals [24-26]. Such compounds as $KAlCl_4$ are so stable that they form even in the vapor [27]. Therefore, for example, in systems KCl–$AlCl_3$ or KBr–$AlBr_3$ to consider $AlCl_3$ or $AlBr_3$ as dielectrics is as impossible as to consider SO_2 a dielectric in the compound K_2SO_4.

Gorenbein is forced to consider low DP and fused systems which contain aluminum halides in this way so as to account for the formation of his "structural groups" in fused salts. However, as shown above, the idea of "structural groups" (as understood by Gorenbein) does not help at all to solve the problem of the concentration of the potential determining ions in a fusion. An explanation for the reason for the transposition of metals in the electromotive force series on the basis of an assumption of the presence in the melt of associates and complexes, shown by different experimental methods, is undoubtedly more reasonable than the use of the "structural groups" assumed by Gorenbein. Among other things, the statement of Gorenbein [1] that investigators have not turned their attention to the possibility of formation of cation complexes in solutions and melts is based on a misunderstanding. Sufficient acquaintance with the review paper of L. N. Antipin [28] would convince him of the contrary. In particular, for the aluminum halides, for which Gorenbein does not recognize cation complexes, the formation of these is possible according to the scheme: $2AlCl_3 \rightleftharpoons AlCl_2^+ + AlCl_4^-$.

For an explanation of some regular changes in the value of the electrode potential in fused salts aside from complex formation, we were attracted to the idea of reciprocal polarization of the ions of the melt and of atom-anion polarization on the surface of the electrode.

In one of his papers [2], Gorenbein tries to connect reciprocal polarizability of ions with the formation of "structural groups." In relation to this question we read the following: "It is known that the polarizability of halogen ions increases from the fluorine ion to the iodine ion. Therefore, the degree of regulation with other conditions equal will be greater for electrolytes with iodine anions. For such solutions the concentration of the potential determining ion will be less; therefore, the corresponding value of the electrode potential is changed, as is actually found." Then follows a reference to a work [29] which reports the results of an experimental study of the potential of decomposition of some metal halides in $SnCl_2$ and $SnBr_2$ as solvents. This work [29] shows that in these solvents the electrochemical series is somewhat different. However, Izbekov and Skobets [29] did not study fluorides or iodides and also did not determine the values for the electrode potentials in fluroides, chlorides, bromides, and iodides. Therefore, the data of these authors can in no way confirm the ideas expressed above by Gorenbein.

Cation	Equivalent conductivity at the melting point			
	anion			
	F^-	Cl^-	Br^-	I^-
Na^+	77.2	133.5	132.0	134.0
K^+	95.5	104.0	124.0	89.0
Ag^+	—	124.2	104.2	85.8
Tl^+	—	46.6	31.7	24.8
Cd^{2+}	—	51.8	32.0	6.4
In^{3+}	—	14.7	6.4	2.3

In connecting polarizability of ions with regulation, Gorenbein once more contradicts himself. As was noted above, according to Gorenbein, conductivity will be higher, the greater the regularity. If, as Gorenbein writes [2], regularity rises in the order fluoride, chloride, bromide, iodide, then the conductivity should rise in the same order. As to how this assumption of Gorenbein agrees with the observed facts is clear from the data on conductivity given in the table.

For the heavy metal halides the conductivity, in spite of Gorenbein, regularly decreases as we go from chlorides to iodides. As to the alkali metal halides, it is difficult to speak of a regular change in conductivity.

According to Gorenbein, the maximum concentration of the potential determining ion should be found for fluorides. Therefore, in fusions of fluorides the electrode potential of metals, it would seem, should be more positive than for the other halides. However, experiment does not confirm this. The electrode potential in fusion of fluorides is more negative than in fusions of iodides [30]. This fact is satisfactorily explained by assuming a reciprocal polarization of the ions and is in sharp contradiction to the ideas of Gorenbein. We find it necessary to remark that the explanation of the transposition of metals in the electromotive force series on the basis of ideas of "structural groups" developed by Gorenbein contradicts a very considerable number of facts.

Thus, the explanation of Gorenbein of the causes of transposition of metals in the electromotive force series in fused salts is implausible in all its assumptions of "structural groups" with their astonishing properties.

SUMMARY

1. The idea of the existence in solutions and fusions of special "structural groups" which have an intrinsic conductivity greater than that of the free ions which compose them, in spite of the statements of E. Ia. Gorenbein, is not derived from the quasi-crystalline theory of liquids and contradicts the present theory of conductivity.

2. The attempts of E. Ia. Gorenbein to explain by his "structural groups" the reason for the transposition of metals in the electromotive force series (for fused electrolytes) are implausible and lead to contradiction of a large number of experimental facts.

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IN MEMORY OF ANDREI IVANOVICH LUN'IAK

On October 15, 1957 in his 76th year, after a heavy and prolonged illness, Andrei Ivanovich Lun'iak died; he was professor of chemistry in the Kazan Medical Institute, a pupil of A. M. Zaitsev.

A. I. Lun'iak was born in St. Petersburg on December 17, 1881. He finished the Odessa Gymnasium in the autumn of 1899 and entered the St. Petersburg Military Medical Academy. From the beginning of his training at the Academy, Lun'iak showed great interest in chemistry, a course which was taught by Prof. A. P. Dianin, under whose instruction Lun'iak made practical experiments in carrying out the different laboratory studies; while still a student in 1903 he completed a scientific study "On the Products of Condensation of Aliphatic Aldehydes with Phenol." This work was presented at a meeting of the Russian Chemical Society, and the Conference of the Military Medical Academy awarded it the Zinin Prize.

When he finished the Military Medical Academy in 1904, A. I. Lun'iak was appointed military physician in Kazan. However, he followed his inclinations and in his free time he continued to occupy himself with chemistry in the laboratory of Prof. A. M. Zaitsev. Later, in 1906, Lun'iak resigned from military service and devoted himself entirely to chemistry, becoming a student in the organic chemistry laboratory of Kazan University. Here, under the direction of A. M. Zaitsev, Lun'iak undertook the synthesis of high molecular weight tertiary alcohols by the action of acid anhydrides with alkyl halides in the presence of zinc and magnesium. At the same time he prepared, at the request of the university and by special permission, to take his Master's examination.

In the spring of 1908, on the recommendation of the Physicomathematical Faculty of the University, Lun'iak was sent for 2 years to Berlin, where he worked in the laboratory of E. Fischer on the synthesis of the dipeptide prolylphenylalanine and its optical isomers. The synthetic dipeptide was identified with the natural one obtained by the hydrolysis of a protein.

When he returned from abroad in 1910, A. I. Lun'iak was appointed privat-docent at Kazan University, where he continued to work on the problems of A. M. Zaitsev and taught a number of courses in the Physicomathematical and Medical Faculties.

In 1912 A. I. Lun'iak was chosen in a competition as adjunct professor in the chair of organic chemistry and agricultural analysis at the Novo-Aleksandrii Agricultural Institute. Here Lun'iak finished his Master's dissertation on the theme "The Action of Organic Zinc Halides on the Anhydrides of Monobasic Acids," which he defended in March, 1914 at Kiev University.

From 1916 to 1924 A. I. Lun'iak was professor of physiological chemistry in the newly opened Perm University where besides his teaching and research he turned to administrative and organizational activities. He

was Dean of the Physicomathematical and Medical Faculties and then served as Rector of the University.

In 1924 A. I. Lun'iak was chosen by competition as professor of technical chemistry at Kazan University and at the same time gave a course in chemical technology in the Institute of Agriculture and Forestry. In 1925 he was chosen Rector of this Institute, and in 1926 Rector of the V. I. Ul'ianov-Lenin Kazan University.

From 1930 A. I. Lun'iak occupied the chair of organic chemistry in the Technological Faculty of the Kazan Chemicotechnological Institute, which was organized in the chemical division of the university. At the same time, with great energy A. I. Lun'iak worked on problems of technology and in 1929 took an active part in organizing a special higher technical school for fats in the Vahkitov Combine. At the same time, for many years, Lun'iak also taught organic chemistry.

In 1936 A. I. Lun'iak was chosen director of the chair of organic chemistry in the Kazan Medical Institute, where he taught chemistry for many years. In 1952 the state of his health forced him to retire but he did not lose interest in the work of the chair and he continued a lively interest in the life of the Institute.

Since he had great organizing ability and inexhaustible energy, Lun'iak knew how to introduce into any subject which he directed a stream of fresh initiative and lively ideas. In 1929 he was one of the active organizers of the 5th Mendeleev Congress which was successfully conducted in Kazan.

A. I. Lun'iak took an active part in the development of chemical industry of the Tartar Republic. The Party and the authorities valued his services highly and awarded him the Order of Lenin and a medal "For his great services in the War of 1941-1945."

The memory of A. I. Lun'iak will always remain in the hearts of his students and co-workers.

List of the Scientific Works of A. I. Lun'iak

1. The Products of Condensation of Aliphatic Aldehydes with Phenols, Zhur. Russ. Fiz-Khim. Obsh. 36, 301 (1904).

2. The Products of Condensation of Aliphatic Aldehydes with Phenols, Zhur. Russ. Fiz.-Khim. Obsh. 38, 466 (1906).

3. High Molecular Weight Tertiary Alcohols. Address at the 2nd Mendeleev Congress (1911).

4. The Action of Organic Zinc Halides and Organic Magnesium Halides on the Anhydrides of Monobasic Fatty Acids, Dissertation (St. Petersburg, 1914).

5. Ueber die Crotonsäureanhydrid, Ber. 42, 915 (1909).

6. Ueber die Einwirkung von Bromessigsäureaethylester und Zink auf die Anhydride der einbasischen Säuren, Ber. 42, 4808 (1909).

7. Deriwate des L-Prolins und des Phenil-alanins

8. The Construction of a Cement-Fertilizer Combine in the Tartar Republic, Kazan Scientific and Economic Institute (Tatizdat, 1930) (with Prof. Bogorodskii and Engineer Sobolev).

9. Prospects for the Chemical Industry in the Tartar Area (Tatizdat, 1932) (with M. A. Iagudin and S. Ia. Arbatov).

V. S. Abramov
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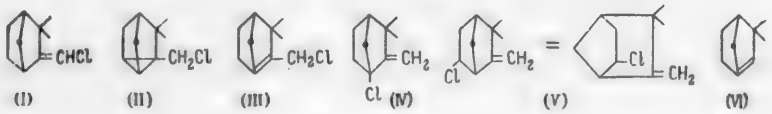
V. A. Frinovskaia

LETTER TO THE EDITOR

G. Chiurdoglu, Ch. Goldenberg, and J. Geeraerts

Recently [1] we reported that in the chlorination of camphene besides chlorides (I) and (II) there was formed the chloride (IV) and not (III) as stated by D. V. Tischenko [2].



(I) (II) (III) (IV) (V) (VI)

The chloride which is the subject of the dispute certainly contains the semicyclic double bond $\diagdown\!\!\diagup C{=}CH_2$: $\nu_{C=C}$ 1647 cm^{-1}, δ 897 cm^{-1}, 2δ 1780 cm^{-1} (infrared spectrum).

This fact at one prevents accepting structure (III)* in accord with the Bredt rule [3], for which, since the work of Prelog [4], the limits of application ($1 \leq n \geq 5$) have become known for bridged compounds.

Speaking more accurately, we can say that with double bonds of the type $\diagdown\!\!\diagup C{=}CH_2$ two compounds (IV) and (V) are possible, both with relatively active chlorine.** We choose chloride (IV) because this substance gives an infrared spectrum identical with the spectrum of α-chlorocamphene, which we have prepared by the method of Meerwein [5].***

The purpose of our work has thus been attained, and we did not try either the synthesis or study of the alcohol ("camphenol") which is formed from this chloride, very possibly, as a result of the Wagner-Meerwein rearrangement.

The fact that Tishchenko obtained a compound $C_{10}H_{16}O_3$, not yet studied, by the oxidation of "camphenol" and not $C_9H_{14}O_2$, did not surprise us at all after the work of Maquestiau [7] which showed that camphene and its analogs like longifolene can be oxidized and are oxidized without loss of a carbon atom.

We assumed however, that our colleague would send us the "camphenol" and the product $C_{10}H_{16}O_3$ so that we could study its structure in our laboratory in Brussels. He told us that he had no more of these two substances.

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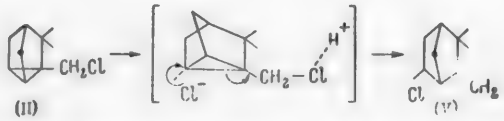
* Chloride (III) is, among other things, a derivative of camphenylene (VI) (mentioned by Snitter [6]) the impossibility of whose existence has been shown in various ways [7].

** According to present views [8] in a molecule like (V) chlorine activates the double bond because it separates the minimum distance. Compound (V) can be obtained in the following way:



(II) (V)

*** The fact that 1-chlorocamphene of Meerwein contains a methylene group united by a double bond can serve, if it is necessary, as a confirmation of its structure.

Discussing the transformation of 1-chlorocamphene (IV) into 1-acetoxycamphene, D. V. Tishchenko considers that this transformation is impossible, since the corresponding carbonium ion should be flat.

The mechanism of the hydrolysis of chloride (IV) is a complex problem. If we assume that the reaction goes by the mechanism $S_N 1$, there should certainly be considerable strain in the cation of the intermediate stage. But if we doubt the possibility of existence of such an unstable intermediate condition with a very short life, then we should all the more exclude any possibility of the existence of a compound of the type of camphenylene (III), (VI), which would contain six coplanar atoms in the field of the double bonds. Finally, as to the last remark, we remind D. V. Tishchenko, that without the help of the spectroscope it would have been impossible in recent years to show the structures of the sesquiterpenes like cedrene, cariophyllene, longifolene, and tricyclovetivene, while over a decade the hydrocarbon $C_{15}H_{24}$ has not yielded to study by classical methods based on dehydrogenations and oxidations [9].

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.